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THE REHABILITATION OF PATIENTS TOTALLY PARALYZED BELOW THE WAIST, WITH SPECIAL REFERENCE TO MAKING THEM AMBULATORY AND CAPABLE OF EARNING THEIR LIVING*

III. Tidal Drainage, Cystometry and Bladder Training

DONALD MUNRO, M.D.†

BOSTON

TIDAL drainage, cystometry and bladder training are interdependent. When properly used in combination they ensure that every patient who has had an injury to the spinal cord, conus or cauda equina and who is intelligent and co-operative will have infallible twenty-four-hour control of urination regardless of the severity of the cord injury. This paper is devoted to a description of the necessary apparatus and a discussion of the technic of these three therapeutic aids in such cases.

TIDAL DRAINAGE

Tidal drainage is a method whereby the urinary bladder can be alternately and automatically filled and emptied, the intravesical pressure constantly maintained at a predetermined level, puddling of residual urine and overstretching or shrinkage of the bladder wall prevented and the bladder maintained in a close approximation to a physiologically normal state even when completely separated from the suprasegmental part of the central nervous system. Although the apparatus, which was first described in 1935,[1] has subsequently been modified and improved, the principle of operation remains the same. Its proper use depends primarily on cystometrographic demonstration of the type of bladder that is to be served. Those hydrodynamic laws that have to do with siphonage determine its activity. Its proper functioning depends on the maintenance of an airtight siphon system during the period of emptying of the bladder.

Siphonage is activated whenever a predetermined intravesical pressure has been reached. The siphon is broken and inactivated by the admission of air as soon as the bladder is emptied. The apparatus is thereby left in such a condition that the cycle can start over again. The control of the admission of air into the system was accomplished in the original apparatus by the use of a water trap. This trap had to be filled before the bladder was filled and before the siphon system could be made airtight; it had to be emptied after the bladder had been emptied before the siphon could be broken. Subsequent improvements led the irrigating fluid directly to the bladder[2] rather than by way of the trap (Fig. 1) and then replaced the trap with a capillary tube.[3] The bore of this tube is too small to permit enough air to enter to break the siphon so long as the system contains any fluid. Through the ingenious use of a four-outlet Carrel–Dakin glass connector, a built-in cystometer is included along with this air vent (Fig. 2). Finally, the air vent and cystometer have been amalgamated[4] by the use of a tube with a large enough bore to act as a cystometer; the apparatus is given the features of the air vent by being made airtight except for the air that enters and escapes through a hypodermic needle thrust through a rubber connection at its top (Fig. 3). All previous models have been abandoned in favor of these last two, which have been given extensive and thorough trials in my clinic. Both are entirely and equally satisfactory if properly constructed, set up and used. Neither is adequate unless used in conjunction with cystometrograms made once a week, or oftener if the occasion requires it.

Construction of the Tidal-Drainage Apparatus

As will be seen from Figures 2 and 3, there are certain parts of the apparatus that are common to both models. These are the following:

A wooden stand, equipped for attachment to the foot or head of the bed, measuring 6½ feet long by 4 inches wide and with a shelf 6 by 6 by 1 inches at either end and on opposite sides. A centimeter scale marked every 0.5 cm., with its zero at the same level as the patient's pubis, is applied to the side of the upright that the lower shelf is on, the zero indicating the bladder level referred to in the figures and the text below.

A 2300-cc. aspirator bottle to which an airtight Murphy dropper that does *not* have a hole in its side is attached by

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an appropriate length of rubber tubing, an adjustable compression clamp controlling the rate of flow through the dropper. The aspirator bottle is strapped in place on the top shelf of the stand and the inlet is closed with a sterile gauze or cotton plug.

A waste bottle corked with a doubly perforated stopper containing short pieces of glass tubing in the perforations.

A No. 16 Fr. soft-rubber rectal tube for use as a catheter in male patients, and either that or a No. 16 Fr. soft-rubber

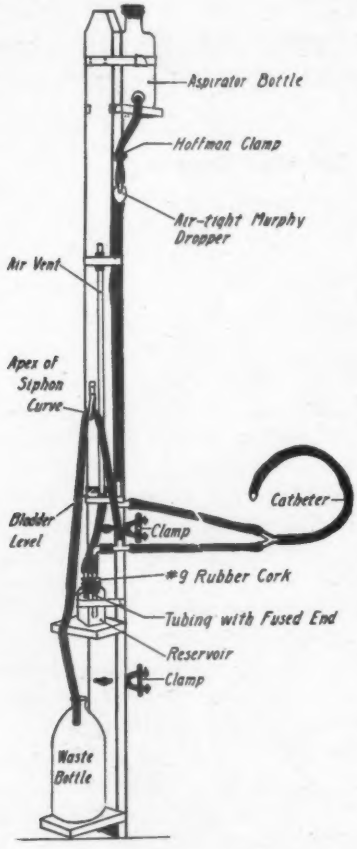

FIGURE 1. *Original Tidal-Drainage Apparatus as Modified by MacNeill and Bowler.*[3]

mushroom catheter for use in female patients, held in place by appropriate adhesive strapping applied to the penis or the pubis respectively. It is important that the maximum size of the catheters be limited to No. 16.[5]

The irrigating fluid used in both models is either Solution M or Solution G.[6] It is sterilized by autoclaving in the usual manner.

To construct the apparatus shown in Figure 2, the following additional material is needed:

A four-outlet (three lateral and one terminal) Carrel–Dakin glass connector.

A glass capillary tube 70 cm. long. This is the air vent and is attached by rubber tubing to the center of the three side openings of the Carrel–Dakin glass connector.

A piece of glass tubing 70 cm. long with an inside bore of about 3 mm. This is the cystometer tube and is attached to the lateral opening that is closest to the closed end of the Carrel–Dakin glass connector by a piece of rubber tubing surrounded by a compression clamp, which is closed when the apparatus is used for tidal drainage and opened when it is used as a cystometer. The Carrel–Dakin connector, with the air vent and cystometer tube attached, is strapped to the wooden upright in such a position that the horizontal center line of the connector is 5 cm. below the bladder level and so that the cystometer tube lies beside the centimeter scale that is on the wooden upright.

A Y tube. The aspirator bottle and attached airtight Murphy dropper are connected by a sufficiently long piece of rubber tubing to one arm of the Y tube, whose upright is inserted in the open end of the catheter. Another equally long piece of rubber tubing is led from the other arm of the Y to the open end of the Carrel–Dakin connector.

A length of small (inside diameter, 3 to 5 mm.) rubber tubing, attached to the third side opening of the Carrel–Dakin connector. This tubing is carried upward to some point higher than the bladder level, passed through a loop of adhesive (this makes the siphon curve) and then led downward and attached to one of the glass tubes in the cork in the waste bottle. The other glass tube remains open. The waste bottle stands on the lower shelf of the wooden upright.

To construct the apparatus shown in Figure 3, the following material is needed in addition to the basic equipment listed above:

A piece of glass tubing 70 cm. long and with a bore of about 3 mm. (the cystometer tube), whose upper end is at-

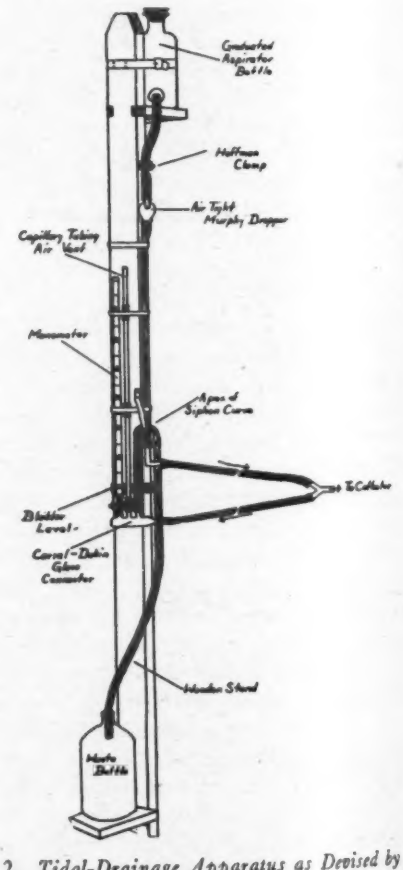

FIGURE 2. *Tidal-Drainage Apparatus as Devised by Stewart.*[3] *The trap is replaced by a capillary tube, and there is a built-in cystometer.*

tached by a short piece of rubber tubing to the outlet of the airtight Murphy dropper.

A hypodermic needle with a patent bore, which is thrust through one wall of the rubber tube. This is the air vent.

A Y tube, one of whose arms is joined by rubber tubing to the lower end of the cystometer tube, the upright being connected to the open end of the catheter with the help of rubber tubing and glass connectors. The cystometer tube

and the attached Y tube are then strapped to the wooden stand in such a way as to place the former beside the centimeter scale with its lower end 5 cm. below the bladder level.

A length of small rubber tubing (inside diameter 3 to 5 mm.), which is led upward from the other arm of the Y tube to some point higher than the bladder level, passed through a loop of adhesive (this makes the siphon curve) and then led downward to be attached to one of the glass tubes in the cork in the waste bottle, the other glass tube remaining open. The waste bottle is placed on the lower shelf of the wooden stand.

In this apparatus the 70-cm. glass tubing serves not only as part of the irrigating system but also as the calibrated arm of a cystometer and, by virtue of the hypodermic needle, as an air vent.

The catheter should be removed, cleaned, resterilized and replaced — if again needed — once a week. Both types of apparatus should be taken down, cleaned and resterilized once a week while in use. It has been the custom in my clinic to attach them to the foot of the bed, but they work equally well when attached to the head or when mounted on a separate upright.

Causes of Functional Failure

No matter which model is used, certain simple precautions must be observed in its operation. Otherwise the apparatus will fail to work. This usually happens because the siphon is broken prematurely. As a result, the bladder either is not permitted to fill sufficiently to raise the intravesical pressure level to the desired height or is not completely emptied at each cycle.

Air leaks, which are the most frequent cause of trouble, generally develop because of either or both of two mistakes. The usual one is to attempt to use a Murphy dropper with a hole in its side instead of the recommended type. Such a hole is excessive when used with either model and especially so with the combined cystometer-tube air vent (Fig. 3), where it is too large to act as a substitute for the hypodermic needle. As a result, too much air enters the system. Even if it is closed with a piece of adhesive tape or bone wax, or both, and whether or not a hypodermic needle is stuck through the adhesive plaster, air leaks through because the suction effect during emptying is strong enough to pull air through the tape and to loosen the wax. The other mistake is to use rubber tubing that has too large an inside diameter for the siphon itself. This applies to both models. During emptying in such a case, the column of liquid flows only down the wall of the tube. Air is thus permitted to rush in through the unsealed center. A tube that is small enough to make the fluid column solid prevents this. In the model illustrated in Figure 2, an air leak may also develop if the clamp at the base of the cystometer tube is not tightly shut.

Another cause of trouble is the formation of a trap in the long catheter connections. This occurs when the tubes are permitted to hang in a loop below the level of the mattress. These rubber tubes should be pinned to the bedclothes on top of the mattress.

Kinks in the connections, clamps that have been put on to stop the flow temporarily and then have not been removed, improperly placed catheters and hypodermic needles occluded by rust are further sources of trouble.

Leakage of urine around the catheter occurs only because the apparatus has not been properly ad-

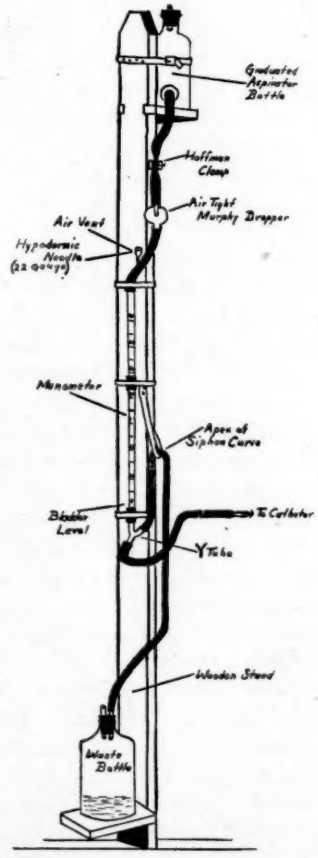

FIGURE 3. *Stewart's Modification of the Tidal-Drainage Apparatus as Modified by Cone and Bridgers.*[4]
A hypodermic needle is substituted for the capillary tube.

justed to the type of bladder it is serving. The remedy is to readjust the tidal-drainage apparatus after a cystometrogram has provided the necessary information regarding the stage of bladder recovery. The one thing not to do for this difficulty is to increase the size of the catheter — this will not stop the leak and will cause urethritis, epididymitis, prostatitis and the like.[5]

Adjustment of Height of Siphon Curve

The proper height of the siphon curve varies with the stage the bladder has reached in its recovery. As pointed out in greater detail below, bladders

associated with significant injuries of the spinal cord or cauda equina pass through four such stages. These are recognizable only by cystometry and vary unpredictably in duration.

Immediately after injury the bladder is atonic. For this stage the siphon curve should be set at 1 or 2 cm. above the bladder level. Recovery progresses through the stages of autonomicity and hypertonicity to the reflex or automatic phase. The siphon curve should be set at 2 to 5 cm. above the bladder level for the autonomous, at 15 to 18 cm. for the hypertonic and at 10 to 12 cm. for the reflex bladder. If the occasion arises — for example, in a patient who is completely unconscious following a severe head injury — when tidal drainage must be used in connection with a normal bladder the siphon curve should be set at 10 to 12 cm. above the bladder level, as in the reflex or automatic bladder.

Cystometry

By cystometry it is possible to determine what the functional activity of the bladder is at the time the cystometrogram is made. As a method of examination it does not pretend to be and cannot be more than relatively exact. If the cystometer and the method of using it approximate as closely as possible the normal physiologic process of filling the human bladder, however, this relative exactitude is sufficient for the purpose at hand. I believe this requirement to be of considerable importance particularly in view of the fact that a number of authors[7–10] have advocated cystometric methods that do violence to this concept.

A normal bladder that is normally innervated receives urine from the ureters constantly and in small increments.[11] The increments are of the order of magnitude of drops. They never, under any circumstances, reach individual amounts of, for example, 10 cc. at a time. An increment of 25 or 50 cc. is physiologically fantastic. The bladder wall, certainly in human beings and probably also in such animals as the dog and cat, reacts in a physiologically normal manner to any normal increase in content. The musculature can and will react also to the admission at one time of larger amounts of fluid but not in the physiologic manner. Inferences regarding the normal activity of the bladder as the result of such abnormal stimuli are not justified and cannot be accepted as evidence for or against any conclusions other than that a purely experimental procedure that has no physiologic basis produces a certain type of muscular reaction. Conclusions based on such cystometric methods — as advocated by Rose,[7] Voris and Landes,[8] Langworthy and Hesser[9] and Langworthy, Kolb and Lewis[10] — cannot therefore be accepted as explanations of normal bladder physiology. All the authors cited advocate cystometric methods in which unit increments of 25 or 50 cc. of fluid are repeatedly introduced into the bladder.

The lethal effect of sepsis on the recovery of skeletal neuromuscular activity that has been previously altered by damage to the central nervous system is well recognized. The neuromuscular mechanism of the bladder can be shown to respond in the same way to this same complication.[12, 13] The deleterious influence of hypoproteinemia on the healing of bedsores, with resultant acute and chronic sepsis, was called attention to in 1940.[14] Many writers have since confirmed this statement, and it is generally acknowledged that proper nutrition is essential for the cure of infection, as well as for the recovery of function and the well-being of patients with cord injuries. Experience with such patients in the Army[15] and elsewhere merely emphasizes this fact. Many of Head's[16] cases in which conclusions were drawn concerning bladder activity were palpably the result of chronic sepsis and probably also of hypoproteinemia. These data can no longer be ignored, and neurophysiologists, such as Fulton,[17] should revise accordingly their concepts of bladder function in man. Interpretation of cystometric evidence without a knowledge of these and other variables is also impossible, and conclusions drawn therefrom are therefore untenable.

Technic

The observations reported herewith have been made with a cystometer that is to all intents and purposes a U tube[18] (Figs. 2 and 3) connected with the contents of the bladder by an unbroken column of fluid. Both ends of the U are open. When a cystometrogram is being made, a standard fill of 400 cc. is used. This fluid is introduced into the bladder at a steady rate of not more than 90 drops a minute. Experiments have demonstrated that this is slow enough to reproduce the physiologic response to the normal filling that takes place by way of the ureters. In every case a catheter that is not of the Foley type is fastened in place in the bladder. The aspirator bottle in either type of tidal-drainage apparatus is replaced by a cylindrical glass container graduated in 25-cc. amounts. The siphon curve is raised to 50 cm. above the bladder level. The cystometer is first filled with an appropriate bland fluid, and all air bubbles are evacuated, after which it is closed off at the point of attachment to the catheter by a clamp. The bladder is then emptied, the catheter is attached to the cystometer, and the clamp is loosened. The compression clamp between the cylindrical container and the airtight Murphy dropper having been opened so that fluid flows at the proper rate of 90 drops a minute and the meniscus in the cystometer tube having been adjusted to the bladder level by the addition of any necessary fluids, it is possible to fill the bladder and read the intravesical pressure simultaneously. The pressure is read in connection with the height above zero of the meniscus in the cystometer tube. The amount of fluid that is in the bladder at any one

time is determined by reading the fluid level in the glass cylinder. Changes in this level of as little as 10 cc. can be approximated with sufficient accuracy to justify recording. Each change in intravesical pressure — whether up or down — that is noted on the cystometer is recorded, and opposite it is placed the amount of fluid that has run over into the bladder up to that point. An additional notation is made whenever there is leakage about the catheter or whenever the cystometer tube or siphon curve overflows. Recordings are continued until 400 cc. of fluid has been run through the apparatus, unless there is reason to fear reflux up the ureters, in which case smaller amounts and lower pressures are used. The catheter is then disconnected from the apparatus, and the bladder is allowed to empty itself with the open end of the catheter held at zero level. This urine is collected and measured. When this process is completed the catheter is lowered and any residual urine that flows out by siphonage is also collected and measured. The operator will then have two parallel columns of figures (one being intravesical pressure readings and the other intravesical cubic centimeters of fluid), as well as the amounts of the residual urine and the urine in the bladder at the close of the procedure.

Interpretation

From these data necessary information regarding bladder function can be obtained. The presence of emptying contractions is indicated when the intravesical pressure reaches or exceeds 50 cm. of water, when there is leakage around the catheter or when either the cystometer or the siphon curve overflows. By noting the amount of fluid that has been delivered to the bladder between each succeeding emptying contraction, it is possible to determine the periodicity and frequency with which the contractions occur.

The curve of basic tonus can also be observed. By subtracting the lowest intravesical pressure from the highest and noting the amount of fluid that has gone through the apparatus, a fairly accurate estimate of the shape of the curve of basic tonus can be obtained. This is a function of the irritability of the detrusor muscle.

The minimal capacity of the bladder is the amount of fill that has collected between the first and second emptying contractions.

The residual urine is best expressed in percentage of fill. To obtain this the amount of residual urine is divided by the sum of the amount of fill (usually 400 cc.) and the amount of urine collected from the bladder at zero level at the close of the procedure.

Temporary elevations of intravesical pressure that neither rise to the height of an emptying contraction nor cause leakage about the catheter are aborted emptying contractions.

The presence of an anal or bulbocavernosus reflex is determined last of all. The test is made by pricking either the perianal region or the glans penis with a pin and observing whether or not there is a reflex contraction of the anus. If there is, the reflex is normal; if there is not, it is abnormal.

By plotting the two columns of figures (centimeters of intravesical pressure and cubic centimeters of intravesical fluid) on co-ordinate paper, a graph of the bladder activity during this experimental fill can be drawn. This is not necessary for adequate interpretation, however. Figure 4 depicts the composite result of cystometric data collected as described above from observations on the bladders of normal persons.

Material

This type of cystometer was used to make observations on 50 persons of varied ages and of both sexes who had completely normal nervous systems and genitourinary tracts, 12 otherwise normal women before and after complete presacral-nerve resection for dysmenorrhea, 22 patients with anatomic cord transections, 16 patients with physiologic cord transections, 35 patients with nontransecting cord lesions, 8 patients with injuries to the sacral cord and conus and 20 patients with various degrees of injury to the cauda equina. In addition, there were 50 patients with less severe cord injuries in whom tidal drainage was used for so short a time that the cystometric observations were not considered useful for the purposes of this paper.

The 101 patients in the selected group with injuries to the cord were, for the most part, studied cystometrically at weekly intervals from the time of admission to the hospital until discharge. Correlation was made between the cystometrograms and the presence and condition of any pressure or bedsores that were present. The trend of the serum protein, as measured by weekly observations of the blood level in milligrams per 100 cc., was constantly observed, and a tendency to fall was forestalled, if possible, by a high-protein reinforced diet and if necessary by the transfusion (multiple when indicated) of whole blood. Sepsis of the genitourinary tract was so insignificant a factor[19] after tidal drainage was used efficiently that it had little or no influence on the observations. Other sepsis and toxemia were given due weight when present. At a conservative estimate, over two thousand cystometrograms on 213 patients with various degrees of injury to the cord, conus and cauda equina have been done in the past twelve years. There can be no doubt that the cystometry has complied with the requirements set down above as minimal.

Observations

In addition to observations that have been made on normal human beings, others have been collected from the human analogue of the spinal animal and under physiopathologic conditions that have not

previously been duplicated. The effects of sepsis, hypoproteinemia, avitaminosis, anemia, physical activity and the like have all been evaluated in relation to the problems of the physiology of micturition and the recovery of the bladder function in these patients. Complications that under other conditions and in other similar series of observations have altered, made unreliable and in some cases vitiated the observers' conclusions either have been recognized as untreatable and the conclusions discarded or have been successfully treated and brought to an end before conclusions were drawn. In the course and partly as the result of these observations it became apparent that in interpreting this group of cystometrograms certain information was essential; other data were not essential but possibly useful, and some were misleading in an estimation of the degree of recovery of bladder function. The essential cystometric information is as follows: the presence of emptying contractions — only normal or reflex bladders develop the classic emptying contractions; the curve of basic tonus, varying from the flat curve of atonicity to the steep gradient of hypertonicity — the former may be present in normal bladders and will be present between the emptying contractions in reflex bladders, and the latter occurs as described below; an anal or bulbocavernosus reflex, which is present only in the absence of spinal shock and when the internal pudic nerve and its spinal-cord connections are intact, indicating either normal voluntary or abnormal involuntary reflex control of the external urethral sphincter; and the capacity of the bladder, which will be a minimal figure varying from the large amount that is limited only by the elasticity of the bladder wall and is collected in atonic bladders to the small amount that is present in bladders that are hypertonic, hypertrophied and shrunken or infected — a minimal capacity below 150 cc. is abnormal.

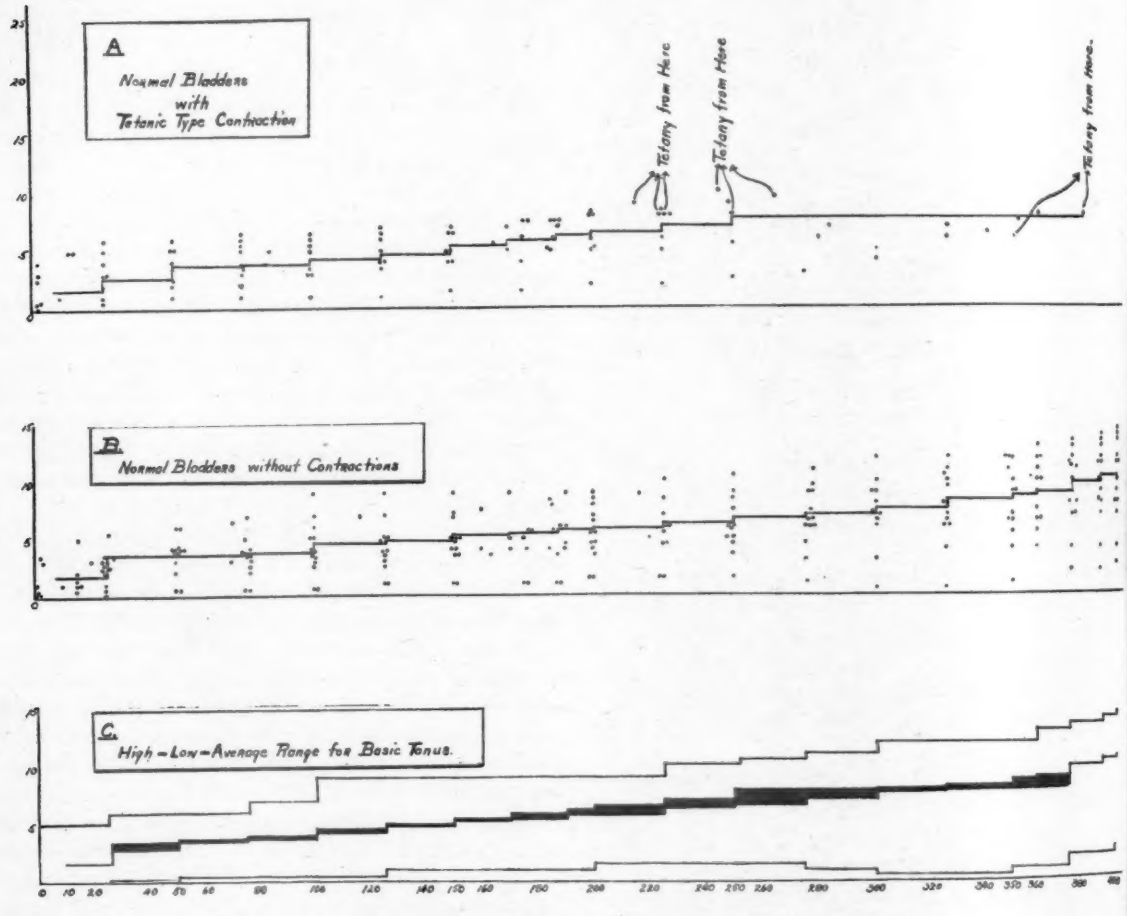

FIGURE 4. *Composite Cystometric Data Relative to the Normal Bladder.*
On the abscissas are recorded cubic centimeters of fill, and on the ordinates centimeters of pressure.

It is useful to know whether or not aborted emptying contractions are present, how much residual urine (expressed in percentage of fill) is present, and

if the patient can tell whether his bladder is empty or full and needs to be emptied.

It may be misleading to determine at what point the desire to void occurs and at what point pain develops. The first is a function of the patient's ability to inhibit emptying contractions and is motivated by such a wide variety of stimuli — varying from inability to urinate while in bed or in the presence of another person to the effect of a total

those advanced in the two previous papers[5, 20] of this series are compiled from observations made on human beings only. Lesions of the spinal cord have been verified by operation, autopsy and clinical observations carried on for a sufficiently long time to establish a stabilized end point and the diagnosis beyond any question of doubt. Cystometrograms have been made in accordance with the physiologic requirements outlined above and by a wide variety

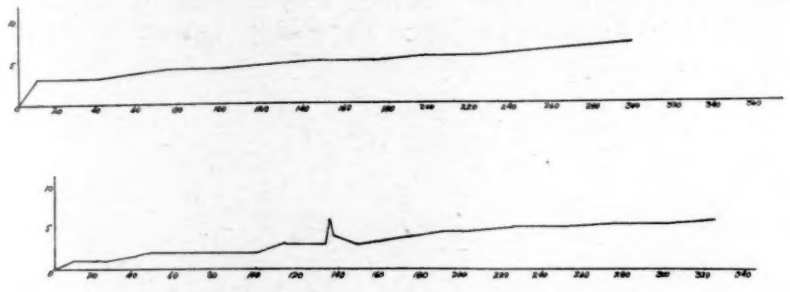

FIGURE 5. *The Graphs of Atonic Bladders.*

The upper one was made ten hours after a cervicodorsal hematomyelia, and the lower one forty-three days after a cervical hematomyelia. In the latter case the atonicity recurred following the development of a major infection.

cord transection — that conclusions based on it are not only unreliable but may lead one astray. The sensation of pain in the bladder wall, if present, means that the organ is being dangerously overstretched. If not present, it may mean the same thing only this time that the danger will be greater

of observers. They strongly suggest the following conclusions. When a human spinal cord is transected either anatomically or physiologically below the fourth cervical and above the second sacral segment, in addition to a complete anesthesia and a total loss of all voluntary motor control below the

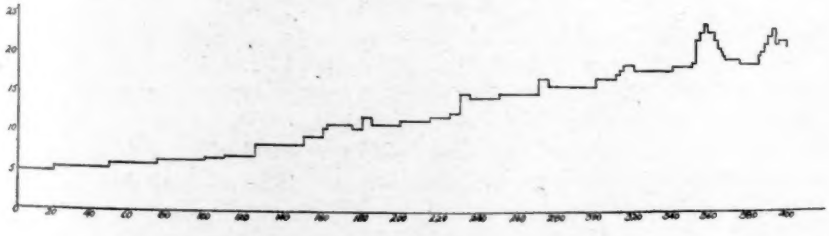

FIGURE 6. *The Graph of an Autonomous Bladder.*

This measurement was made twenty-three days after concussion with transection of the dorsal cord. Aborted emptying contractions are present.

because it is unrecognizable. In addition, it may be pointed out that any interpretations of the physiology of micturition that depend even in part on observations made by the patient and that require an intact nervous system are valueless in the face of an anatomically or physiologically transected spinal cord. The observer who is accustomed to rely on such observations in his clinical work will find himself without them and at a loss in the type of case in which he needs cystometrography most.

The interpretations presented herewith as well as

level of cord injury, the immediate response of the bladder is to become atonic (Fig. 5). The detrusor muscle does not contract at all. The internal sphincter closes tightly and remains closed and unresponsive to any physiologic stimuli during this phase. The external sphincter is relaxed, and the anal and bulbocavernosus reflexes are abolished. Any emptying that occurs is only the result of leakage through the contracted internal sphincter and takes place because of the elasticity of the bladder wall and not by virtue of any contractile effort on its part. The

bladder capacity is limited only by this elasticity. Bladders that have advanced beyond this stage toward recovery will regress to it in the presence of spinal shock, exhaustion, sepsis, toxemia and hypoproteinemia (Fig. 5). The length of time that a bladder remains in this atonic stage depends on these complications, the severity of the injury and the efficiency of the treatment.

The next stage toward recovery is characterized by the development of ineffective aborted emptying contractions (Fig. 6). The level of basic tonus is slightly higher than that in an atonic bladder. The internal sphincter is tightly closed and only partially opens in response to the inefficient aborted emptying contractions of the detrusor muscle. The bulbocavernosus and anal reflexes may return. There are no emptying contractions. This stage may be extremely short and will be missed if cystometrograms are not made frequently enough. The bladders discharge small amounts of urine frequently. Their capacity is at first large but becomes increasingly smaller as hypertrophy of the muscular wall develops. The bladders regress to the atonic stage for the reasons given above. The length of time that the bladder remains in this stage again depends on any complications and the efficiency of treatment, but not on the severity of the injury. This is the autonomous stage, so called because it is believed but not proved that the neural control is exerted by way of an intramural autonomous plexus.

The third stage toward recovery is the hypertonic. This is characterized by something approximating tetany of the detrusor muscle (Fig. 7). It is in a nearly constant state of contraction; the curve of basic tonus is steep, and the intervals between emptying contractions are extremely short. The internal sphincter reacts physiologically, opening with each emptying contraction and closing in the intervals. The external sphincter responds reflexly, and the anal and bulbocavernosus reflexes are present. The bladder capacity as measured by the amount of urine stored between emptying contractions is small. This stage is often of short duration and either regresses toward atonicity or progresses to the reflex stage. An acutely infected but otherwise normal bladder may give a cystometrogram that is indistinguishable from one made during this stage. Normal uninfected bladders exhibit these characteristics just before emptying if they are distended beyond normal limits but have not been so stretched as to have become atonic (Fig. 4).

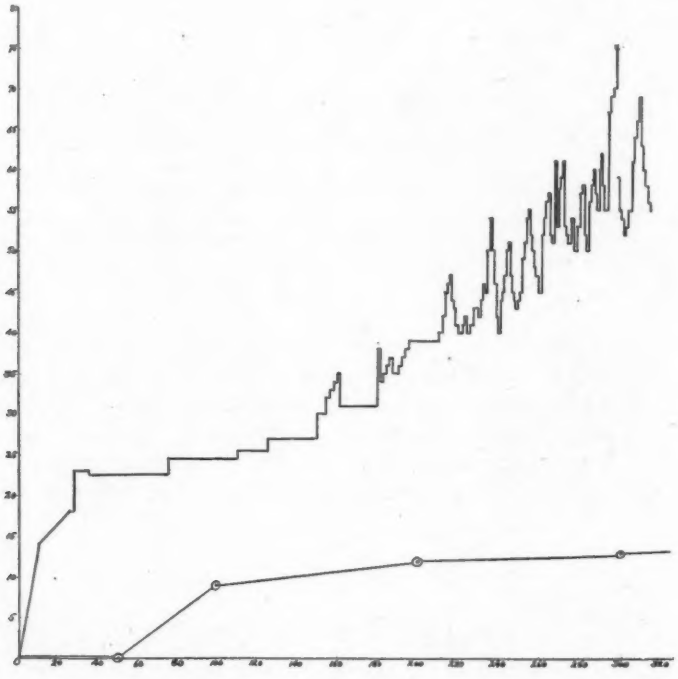

FIGURE 7. *The Graph of a Hypertonic Bladder.*
This graph was made five days after compression of the lumbosacral cord.

The final stage is that of the reflex bladder (Fig. 8). In small children who have not yet learned to obey the dictates of civilization this represents normal bladder activity. Increase in capacity and training in the inhibition of emptying contractions pre-

duce the control that is apparent later as normal adult micturition. Under certain conditions, however, this inhibitory ability can be lost again, the normal bladder reverting to reflex activity in the absence of any physical impairment of its nervous connections. Emotional stress, such as extreme fear of death or bodily harm, may so relax the inhibitory effect exerted by the higher centers that the person experiencing such an emotion finds himself — if the bladder has not been emptied just previously — wet with urine once the danger is passed. I am informed that this was not an infrequent experience during the worst London air raids. Coma, if sufficiently deep, produces the same chain of events; if it is less profound, and even though the victim is out of conscious touch with his surroundings, inhibitory control continues to be exerted, however, and the bladder is prevented from emptying. Convulsive seizures with the profound coma and loss of "sphincter control" of grand mal, on the one hand, and the momentary unconsciousness without soiling of the petit-mal attacks, on the other, as well as the variations between, illustrate these phenomena in all degrees.

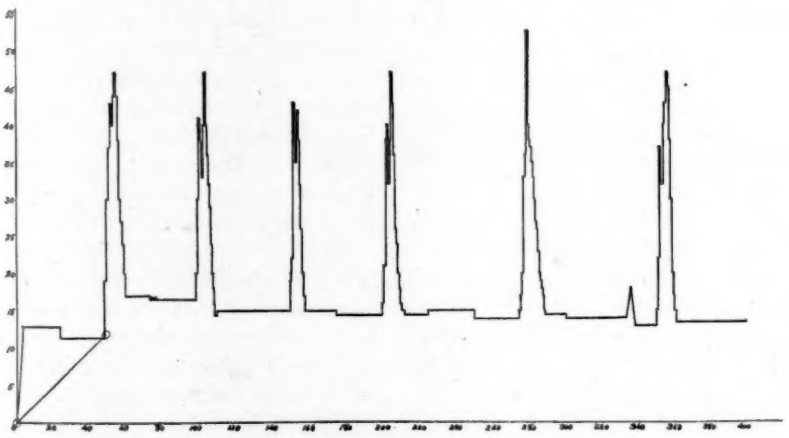

FIGURE 8. *The Graph of a Reflex Bladder.*
This measurement was made seven months after concussion with transection of the dorsal cord.

Cerebral injuries, although not so clear cut on account of the associated central-nervous-system damage, provide similar examples. The deeply comatose patient empties the bladder of large amounts of urine at rare, fairly evenly spaced intervals. The bladder functions on a pure reflex plane, empties completely with each emptying contraction and is deprived of all inhibitory influences. As the condition improves and the coma lessens, the type of micturition changes, and the patient begins to pass small amounts of urine often and at irregular intervals. Catheterization easily demonstrates that this overflow incontinence is the result of an inhibitory effect exerted to the point of overdistention and caused by a subconscious realization that bed is not the place in which to urinate. The restlessness and struggles to get out of bed that persist until a urinal is put in place and the bladder emptied completely of a large amount of urine, only to be followed by a period of quiet or sleep, afford verification of this phenomenon. Indeed, the change from the periodic urination of large amounts that is characteristic of reflex micturition to the irregularly spaced, frequent discharge of the small amounts of overflow incontinence is often an early and always a reliable sign of the lessening of unconsciousness and an improvement in such a patient's condition and vice versa.

Reflex bladder activity is also a function of the anatomically and physiologically transected cord. Under such conditions, it is the best end result that can be attained, and bladder training as described below is merely a method of making practical use of this phenomenon. It is this activity that has been referred to in the past as the "automatic bladder." In nontransecting injuries, it is not and should not be considered an end result. In these injuries the activity is analogous to that of the reflex bladder of the normal infant. Further training enables the patient to regain the normal inhibitory control just as the child does as he grows older. In this reflex stage the detrusor muscle contracts reflexly and completely in response to the sensory stimulus provided by the stretch of a critically filled bladder. During the fill and before the accumulation of this critical amount of urine, any emptying contractions are aborted in favor of a stretch reflex and consequent increase in the cubic capacity of the organ. The internal sphincter remains closed until the emptying

contraction takes place, when it opens and permits urine to escape into the posterior urethra. This, in turn, acts as a sensory stimulus that causes the external sphincter to relax reflexly from its previously contracted closed position. The bulbocavernosus and anal reflexes are present. If the cord injury is nontransecting the patient also has the ability to relax and contract voluntarily the external sphincter. If the injury is a transecting one, this voluntary control is permanently lost. If the bladder has not been allowed to shrink during the early stages of its recovery from atonicity, its critical capacity varies from 200 to 400 cc. or more. When it does empty, all the contents are expelled. Reflex emptying in cases of transected cord may also be initiated -- regardless of the amount of the contents — by contraction of the abdominal muscles, stimulation of the abdomen, thigh and other areas of the leg, catheterization, movement of the bowels and change in position. Facilitation of micturition as a part of the "mass reflex" described by Head[16] is, according to my observations, no more than an indirect and coincidental effect. In patients whose abdominal musculature has been paralyzed because of the destruction of the lower dorsal roots but in whom the mass reflex is typical and active, there is no such facilitation. I have seen two such cases. Also, as noted in a previous paper,[20] in patients in whom the mass reflex has been inactivated by anterior rhizotomy, facilitation of micturition is still present on a reflex level in response to stimulation of the skin of the thigh and an increase in intra-abdominal pressure, as well as to intravesical stimulation acting alone and without any external aid and caused by the collection of a critical amount of fill within the bladder. I have had experience with 10 such cases. Regression toward atonicity takes place in the presence of infection, toxemia, exhaustion, a major operative procedure, hypoproteinemia and so forth. A decrease in capacity and hence an increase in the number of emptying contractions develop in the presence of cystitis, vesical calculi and prolonged suprapubic drainage. Urinary retention despite the presence of otherwise efficient emptying contractions has been shown to be caused by hypertrophy or fibrosis[21–24] with a pseudo-median-bar formation of the internal sphincter. Although the evidence is not conclusive, it is probable that this retention has its origin in injudicious early treatment of the bladder and is a complication of too prolonged and constant catheter or suprapubic drainage. It has occurred only twice in my series of 40 cases with anatomic and physiologic transections. One was in a patient who had been subjected to suprapubic drainage for five months followed by catheter drainage for the same length of time. The other had catheter drainage for three months following the accident. For two years and nine months thereafter he had no bladder treatment of any kind. Many of the other patients in this group, however, had as long or longer periods of suprapubic or catheter drainage without the development of this complication.

Destructive lesions that are complete and involve the sacral segments or roots or the parasympathetic plexuses, and hence completely denervate the bladder as far as its central connections go, force the bladder to depend on the intramural plexus for neuromuscular control. This ability develops after the bladder has recovered from the atonic stage. The resultant bladder activity duplicates that described above under the term "autonomous bladder" (Fig. 6). This is the best physiologic end result that can be obtained in such cases. Because of the total denervation it is impossible to impose bladder training on these patients. That does not mean, however, that the patients must accept a contracted bladder that will hold only 30 or 50 cc. and that leaks virtually constantly. Even in the face of total denervation, the bladder capacity can be maintained at normal by the prompt use of tidal drainage in the preconvalescent bed stage. When the patient is ambulant, unfailing twenty-four-hour control can be established if the patient continues to wear an indwelling catheter. During the day the catheter is kept closed by a clamp except when the bladder is emptied at intervals of three or four hours. During the night, while the patient is in bed, the catheter is opened and attached to a tidal-drainage apparatus with the siphon curve set at 10 to 12 cm. The bladder wall is thus kept from hypertrophy and contraction, and the patient is enabled to keep himself dry and clean at all times. The catheter is removed, cleaned, resterilized and replaced aseptically once a week, and the apparatus taken down, cleaned, resterilized and reassembled after the same interval. Solution M or Solution G[6] is used as an irrigating fluid. Any person of ordinary intelligence can without difficulty be taught the proper care of himself and this apparatus.

Impulses reaching the bladder by way of the sympathetic as distinguished from the parasympathetic and somatic nervous systems have no influence on the function of storage or discharge. This was first enunciated by Denny-Brown and Robertson.[25] Through the kindness of Dr. Frank A. Pemberton I was enabled to make preoperative and postoperative cystometric observations on 12 otherwise normal women whose presacral plexuses were totally removed because of dysmenorrhea. In every case the bladder activity was unaltered following the sympathetic denervation. Similar findings have been reported by Marshall and Kennedy.[26] In the light of this evidence, Learmonth's[27] conclusions, and Fulton's[17] acquiescence in them, regarding the antagonistic control of bladder activity so far as it refers to the sympathetic-nervous-system innervation of the bladder, cannot be accepted any longer. Denny-Brown and Robertson's[25] original contention that the effect of the sympathetic nervous system

on the bladder concerns the transmission of pain from that organ appears to be confirmed.

Bladder Training

Bladder training should be necessary only in patients with anatomically or physiologically transected cords. It will be effective only if the patient takes an intelligent interest in the problem and cooperates. If the bladders have been properly cared for from the time of injury, such training is not necessary with nontransecting cord injuries. It is ineffective in patients with destructive lesions of the sacral cord or roots and the parasympathetic plexuses. It cannot be imposed on and is not successful in any patient who is mentally deficient or unco-operative or who has a suprapubic or perineal cystostomy, bladder obstruction from any cause, an infected bladder, vesical or renal calculi, pyelitis or pyelonephrosis, general sepsis, toxemia, exhaustion, debilitation, hypoproteinemia, avitaminosis, large unhealed bedsores and the like. The bladder activity must be of the reflex type, and the bladder capacity at least 200 cc.; in patients with an active mass reflex the lower half of the abdominal wall must have been paralyzed either because of appropriate thoracic-root destruction as part of the injury or following operative bilateral anterior dorsolumbar rhizotomy. To prevent genitourinary infection the fluid intake must not be allowed to fall below 3600 cc. in twenty-four hours during the period of training. Bladder training is much easier when the patient is ambulant in splints and with the aid of crutches, but its initiation should not be postponed on that account. The patient must have sufficient use of his hands to clamp and unclamp the catheter, must have a watch, must understand the elements of the problem he is faced with, must be co-operative and must be willing to assume full responsibility for the solution of that problem. With these requirements met, all that is necessary is patience and perseverance on the part of both the patient and the doctor.

Control of micturition is possible in the presence of a transected cord because the bladder, if not otherwise altered, can be distended to a point where it contains from 200 to 400 cc. of urine before emptying and because an emptying contraction can be initiated as a reflex response to appropriate sensory stimuli at any time previous to that point. By appropriate regulation of the fluid intake, the time that elapses before this amount is collected in the bladder can also be predetermined. By emptying the bladder reflexly under controlled conditions immediately before the contents reach the critical level, soiling with urine at unexpected times can be prevented.

Technic

The first stage in the training is to condition the bladder so that it will distend to the point where it holds 200 cc. or more without developing an emptying contraction. This phase can and should be started while the patient is still in bed and as soon as the bladder activity has become reflex in type. To do this, the catheter is left in place but disconnected from the tidal-drainage apparatus and clamped off for an hour and a half at a time. At the end of each of these periods the catheter is opened, the open end placed so as to empty into a urinal and the bladder made to contract by appropriate reflex stimulation such as massage of the abdomen, scratching of the thigh or any similar procedure that is effective. Forcible expulsion of the contents by pressure through the abdominal wall should not be practiced under any circumstances. The fluid intake is adjusted so that no fluid is taken between 7:00 p.m. and 7:00 a.m. During the other twelve hours 300 cc. should be ingested every hour, preferably on the hour. This fluid intake remains the same throughout the training period and thereafter until full adjustment and control are obtained. The patient should be held responsible for draining his own bladder at proper intervals during the day. At night the catheter should be attached to the tidal-drainage apparatus. After he is able to go for a week without leakage between emptyings, the interval should be increased to two hours. The process is repeated until the same requirement can be successfully met. After this, the interval is increased to two and a half hours and then to three hours. The greatest difficulty is usually encountered in making the change from an hour and a half to two hours. If leakage occurs at that time or at any other change, the patient should be put back on the next shortest interval for another week or so and the shift upward tried again.

When the patient can successfully manage a three-hour interval without leakage, he should be taken off tidal drainage at night. Instead he should be awakened and made to empty the bladder every two hours until a week has passed without leakage and subsequently every three hours. He will then be able to retain the bladder contents for three hours at a time without leakage day and night, but the catheter will still be in place. The activity of the detrusor muscle has been conditioned, but not the sphincters. To attain that end, the catheter should be removed entirely and the time interval between emptyings cut back again to an hour and a half. The intervals are then increased as indicated above, but without the catheter. It is during this stage that obstruction by a spastic or hypertrophied internal sphincter becomes evident if it exists. Such a condition occasionally requires resection, but this should not be done until a serious effort has been made and enough time allowed to elapse for the sphincter to correct its own spasticity. Any other obstruction to emptying must be corrected at once and before the training can be continued. It is about this time also that the patients begin to be ambulant. This

change from the recumbent or sitting to the erect position also alters the bladder activity. It is often found that control of micturition, which is entirely satisfactory with the patient erect, fails miserably when he returns to bed. Increased exercise, such as greater agility in using crutches, may also cause temporary intermittent leakage. Persistence in practice and repetition of the earlier training stages, even perhaps to the extent of catheter replacement, will overcome all these difficulties sooner or later, particularly if an increase in ambulation is insisted on. It is also helpful if the patient makes a practice of using the toilet rather than the urinal at each bladder emptying. The position of the body and possibly also the psychology of urinating in such surroundings appears to be conducive to greater efficiency in micturition. In especially difficult cases much help can often be obtained by making the patient keep his own intake and output chart. This should include a time schedule as well.

Complications

Once the patient has reached the stage where he can go for three hours without urinating or leaking during both day and night, he can be allowed to go through the night without being awakened at all or, at most, only once. The daytime interval can also be extended from half an hour to an hour if the need arises. Under no circumstances should the interval between drainages be shortened — such a procedure will quickly cause regression of bladder function. Any unexpected break in efficiency should lead to prompt investigation of the cause. One of my patients was found to have a vesical calculus that had been entirely asymptomatic until the patient was well past the first stages of ambulation. Sudden inability to control micturition in another case was found to have been caused by a small papilloma that had developed without my knowledge and in spite of previous cystoscopic examinations while the patient was under treatment for a cord injury. Removal of the stone and fulguration of the papilloma permitted both patients to regain twenty-four-hour control of micturition.

Successful bladder training can be acquired by any patient with a transected cord if the requirements discussed above are met. It is acquired much more easily and rapidly, however, if the bladder is kept in a state of physiologic normalcy during the immediate post-injury convalescence by the proper use of tidal drainage supplemented by the necessary number of cystometrograms. As pointed out above, an automatic bladder, although better than a contracted or permanently drained bladder, cannot be considered a satisfactory end result. It is merely a preliminary stage in the return of bladder function and should be recognized as a condition that can be transmuted into unfailing twenty-four-hour control of micturition if the physician is alert to the possibilities and the patient intelligent and co-operative.

Patients with denervated bladders (destructive lesions of the sacral cord or roots or parasympathetic plexuses) can have the same control but must be willing to wear a catheter constantly and to use tidal drainage at night. They are trained in the manner described above to increase the intervals between bladder drainages from an hour and a half to three hours, except that they never reach the stage of training without catheters and that they are not awakened at night. It is possible that resection of the internal sphincter[21] will eventually prove to be the solution that will permit removal of the indwelling catheters and abandonment of the tidal-drainage apparatus in these cases.

No satisfactory method of treating the urinary difficulties of patients with paralyzed hands has been evolved, other than to have an attendant open and close the catheters during the first part of the training period. Manpower shortage has made this impractical, but if that difficulty can be overcome, there is no reason why such patients should not eventually attain bladder control once the catheters can be removed. After that, the reflex emptying that follows sensory stimuli set up by scratching the abdomen or thigh will be within the scope of their limited activities. Fortunately, these cases are rare, because patients with transections of the middle and lower thirds of the cervical cord — whether anatomic or physiologic — rarely survive long enough to reach the stage where bladder training is indicated, and if they do, it is of little practical value to them because of the impossibility of ambulation. So long as they are bedridden, they do better on tidal drainage. Patients with nontransected cases with hand paralysis traceable to cord changes associated with hematomyelia will have normal bladder activity if their bladders are properly treated from the start. The only problem is to obtain urinals that they can use when necessary. With normal control of micturition, accidents can usually be avoided because of the leeway permitted by virtue of the ability to inhibit an emptying contraction for a reasonable and possibly a considerable period.

Patients with cauda equina injuries that do not denervate the bladder may nevertheless have sufficiently disabling bladder symptoms to prevent a normal social and work life. Cystometrically, the only variation from normalcy is a decreased capacity and evidence of hypertonicity in that emptying contractions develop more frequently than normal and the curve of basic tonus is steeper than normal. The bladder symptoms are usually extreme urgency, frequency, dribbling and unexpected major leakage. In my experience all these patients have sustained such injuries in civil life. There has been a major fracture of a lumbar vertebra with the escape of quantities of free blood into the lumbar subarachnoid space. Because this possibility is usually not

only not investigated but not even considered, this blood is permitted to remain undisturbed only to organize and produce fibrotic adhesions, which compress and deform the cauda equina.[28] Varied symptoms of radiculitis develop, the usual ones being pain alone or in combination with the type of urinary difficulty described above. Clinical evidence suggests that to correct the bladder symptoms the radiculitis must be relieved and the bladder stretched if it has shrunk. The first is accomplished by a decompressive lumbar laminectomy in which the five laminas overlying the cauda equina are removed, the dura opened for the full length of the wound and any neurolysis that may be possible carried out. The wound is then closed without drainage and without closing the dura. Preoperative investigation of the dynamics of the spinal cerebrospinal fluid is essential and usually reveals a partial and often a complete dynamic block. The patient is put on tidal drainage adjusted to meet the requirements of the cystometric findings and to stretch the bladder if necessary. This is continued until the capacity has been raised to over 200 cc., after which bladder training as described above is instituted. Following this procedure, which has been carried out in 14 such patients, all of whom were unemployable on account of their urinary difficulty, all but 2 have returned to regular employment and all are free of urinary symptoms.

Summary

Two types of apparatus for tidal drainage are described, and directions given for their construction.

The physiology of micturition is briefly discussed.

A method of cystometric examination of bladder function in normal bladders and in those rendered abnormal by spinal-cord, conus and cauda-equina injuries is described, and an interpretation of the findings is given.

A method of bladder training that will permit unfailing twenty-four-hour control of urination, even in the face of an anatomic cord transection or total denervation of the viscus, is discussed in detail.

References

1. Munro, D., and Hahn, J. Tidal drainage of urinary bladder: preliminary report of this method of treatment as applied to "cord bladders" with description of apparatus. *New Eng. J. Med.* **212**: 229-239, 1935.
2. MacNeill, A. E., and Bowler, J. P. Irrigation and tidal drainage. *New Eng. J. Med.* **223**:128-132, 1940.
3. Stewart, O. W. Neurogenic bladder: combined tidal irrigator and cystometer. *Lancet* **1**:287-289, 1942.
4. Cone, W. V., and Bridgers, W. H. Combined tidal irrigator and cystometer for management of paralyzed bladder. *Surg., Gynec. & Obst.* **75**:61-66, 1942.
5. Munro, D. Rehabilitation of patients totally paralyzed below waist: with special reference to making them ambulatory and capable of earning their own living. II. Control of urination. *New Eng. J. Med.* **234**:207-216, 1946.
6. Suby, H. L., and Albright, F. Dissolution of phosphatic urinary calculi by retrograde introduction of citrate solution containing magnesium. *New Eng. J. Med.* **228**:81-91, 1943.
7. Rose, D. K. Determination of bladder pressure with cystometer: new principle in diagnosis. *J. A. M. A.* **88**:151-157, 1927.
8. Voris, H. C., and Landes, H. E. Therapy of neurogenic bladder. *J. Internat. Coll. Surgeons* **5**:206-215, 1942.
9. Langworthy, O. R., and Hesser, F. H. Experimental study of micturition released from cerebral control. *Am. J. Physiol.* **115**:694-700, 1936.
10. Langworthy, O. R., Kolb, L. C., and Lewis, L. G. *Physiology of Micturition: Experimental and clinical studies with suggestions as to diagnosis and treatment.* 232 pp. Baltimore: Williams and Wilkins, 1940.
11. Starling, E. H. Muscular mechanisms of urinary tract. In *Text Book of Physiology.* Edited by E. A. Schäfer. Vol. 2. 1365 pp. Edinburgh and London: Pentland, 1900. Pp. 338-347.
12. Munro, D. "Cord bladder": its definition, treatment and prognosis when associated with spinal cord injuries. *J. Urol.* **36**:710-729, 1936.
13. *Idem.* Treatment of urinary bladder in cases with injury of spinal cord. *Am. J. Surg.* **38**:120-136, 1937.
14. *Idem.* Care of back following spinal-cord injuries: consideration of bed sores. *New Eng. J. Med.* **223**:391-398, 1940.
15. *War Department Technical Bulletin.* No. 162, May, 1945.
16. Head, H., and others. *Studies in Neurology.* 862 pp. Vol. 2. London: Henry Frowde, 1920.
17. Fulton, J. F. *Physiology of the Nervous System.* Second edition. 614 pp. New York: Oxford University Press, 1943.
18. Munro, D. Activity of urinary bladder as measured by new and inexpensive cystometer. *New Eng. J. Med.* **214**:617-624, 1936.
19. Badal, D., Munro, D., and Lamb, M. E. Clinical significance of bacteriuria in patients with spinal-cord injuries. *New Eng. J. Med.* **230**:688-693, 1944.
20. Munro, D. Rehabilitation of patients totally paralyzed below waist: with special reference to making them ambulatory and capable of earning their own living. I. Anterior rhizotomy for spastic paraplegia. *New Eng. J. Med.* **233**:453-461, 1945.
21. Pierson, E. L. Transurethral resection of internal sphincter in certain type of cord bladder. *New Eng. J. Med.* **213**:50-54, 1935.
22. Van Duzen, R. E. Operations for urinary control of neurogenic bladders. *J. Urol.* **53**:565-571, 1945.
23. Band, D. Cystometry. *Brit. J. Urol.* **17**:1-25, 1945.
24. Lewis, L. G. Discussion of Hanlon, R. E. Treatment of urinary incontinence in vesical paralysis. *J. Urol.* **53**:572-579, 1945.
25. Denny-Brown, D., and Robertson, E. Graeme. On physiology of micturition. *Brain* **56**:149-190, 1933. State of bladder and its sphincters in complete transverse lesions of spinal cord and cauda equina. *Ibid.* **56**:397-463, 1933.
26. Marshall, S. F., and Kennedy, R. J. Postoperative results following presacral neurectomy (excision of hypogastric plexus) for dysmenorrhoea. *S. Clin. North America* **25**:518-529, 1945.
27. Learmonth, J. R. Contribution to neurophysiology of urinary bladder in man. *Brain* **54**:147-176, 1931.
28. Munro, D. Treatment of patients with injuries of spinal cord and cauda equina preliminary to making them ambulatory. *Clinics* **4**: 448-474, 1945.

THE RESULTS OF SURGICAL TREATMENT IN GRAVES'S DISEASE*

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THE introduction into this clinic by Astwood[1] of thiouracil and other potent antithyroid drugs for the medical treatment of Graves's disease resulted in a challenge to the concept that this condition is best treated surgically. Thus, there is a growing divergence of opinion concerning the relative merits of medical and surgical therapy in hyperthyroidism.

As a contribution to the discussion of this problem, a study has been made of the results of surgery for a period during which the performance of adequate subtotal thyroidectomy, combined with the proper use of iodine and other preoperative and postoperative measures, was the accepted method of therapy. This study is a review of all the cases of Graves's disease — that is, toxic diffuse goiter — surgically treated at the Peter Bent Brigham Hospital from 1933 through 1940. In the eight years reviewed, operations were performed in 149 cases in which a pathological report of diffuse hyperplasia of the thyroid gland was made. It is believed that such an analysis will establish a pattern against which similar controlled observations on patients treated with thiouracil may be compared.

It is the practice of the Surgical Service to follow these patients at regular intervals, and a majority of them were seen in the follow-up clinic of the hospital over a period of several years. For the purpose of this analysis, no result was considered satisfactory unless the patient had been under observation for at least six months after operation. When an unsatisfactory result was immediately apparent, however, this has been indicated, even though the patient's condition could not be checked through a minimum of six months. Nineteen patients whose condition at discharge was satisfactory failed to maintain contact with the clinic for a sufficient length of time to allow their final status to be evaluated.

Hypothyroidism after thyroidectomy was encountered in 18 cases. In 9 of these the classic signs of myxedema were found, the metabolic rate in 7 cases ranging from —31 to —47 per cent. The other 9 patients suffered from mild hypothyroidism. In all these cases the condition was well controlled with the administration of thyroid, and the patients eventually led useful and comfortable lives.

Vocal-cord paralysis was noted immediately following the surgical procedure in 7 cases, in 3 of which it was a single complication. In 1 case, which occurred after a first-stage hemithyroidectomy, the patient refused the second stage. Six patients had temporary unilateral paralysis on the basis of symptoms and postoperative examinations.

Four patients showed symptoms of hypoparathyroidism. In one there was evidence of permanent parathyroprivia, on the basis of symptoms and of blood calcium and phosphorus levels. This patient was symptomatically controlled on vitamin D. The case was unusual in that preoperatively tetany could be induced by hyperventilation. One patient was followed for two months, at the end of which he had recovered from the tetany and did not return to the clinic; in addition to mild hypoparathyroidism, this patient sustained a vocal-cord paralysis and mild hypothyroidism. The third patient apparently suffered only a partial parathyroidectomy, since the symptoms of tetany disappeared five days after the operation. The fourth patient lost all signs of tetany within six months and continued in good health for at least eight years.

Persistent exophthalmos was observed in 13 cases. In only one of these did progression of the exophthalmos occur, and the patient was treated by the Naffziger procedure. One patient had marked unilateral, and one marked bilateral exophthalmos; in neither was it progressive. The remaining 10 patients had mild, persistent exophthalmos, without other postoperative difficulties.

Six patients experienced recurrence of thyrotoxicosis eight months to four years after operation. In 2 of these cases prolonged treatment with iodine induced permanent remission. Two patients underwent second operations, one experiencing a good result and the other disappearing from the clinic after the operation. There was no record of the courses in the remaining patients with recurrence after the diagnosis was established.

Five additional patients experienced persistence of the disease after operation. Two of these were referred to radiologists for radiation therapy. Two patients with persistent disease could not be followed. The fifth was of special interest in that three operations were performed. At the first, 76 gm. of thyroid tissue was removed, a less extensive procedure than was considered optimal being carried out because of the poor state of the patient. She was observed to have persistence of the disease but for seven years refused further treatment. Then

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she underwent a second operation, during which 83 gm. of tissue was removed. The postoperative course was difficult, with true thyroid storm, and again the disease persisted until the final operation, when 50 gm. of tissue was removed. Following this, except for a transient unilateral vocal-cord paralysis, this patient made a complete recovery.

Thompson and his colleagues[2, 3] have presented many of the adequate data on recurrent and persistent hyperthyroidism, reporting an incidence of postoperative thyrotoxicosis in 19.5 per cent of cases at the Massachusetts General Hospital and in 17.5 per cent at the Presbyterian Hospital in Chicago. The data from the Massachusetts General Hospital indicate that this rather high incidence was attended by a low incidence of true myxedema (1 per cent). The studies made in the series at the Peter Bent Brigham Hospital reveal that 8.3 per cent of patients showed recurrent or persistent thyrotoxicosis.

The figures cited above indicate that the results reported from the Peter Bent Brigham Hospital are probably representative of those to be expected from other hospitals where general surgery is practiced. They are also in accord with the data concerning postoperative thyrotoxicosis gathered by Fulton, Schnitker and Cutler[4] in this hospital in 1938.

Four patients died as a result of the operation. The ages ranged from forty to forty-nine years. Two deaths were due to postoperative thyroid storm, and one to hemorrhage into the wound with cessation of respiration. Each of these patients had responded favorably to treatment with iodine and bed rest prior to operation. The fourth fatal case occurred in a woman who refused further treatment after an adequate response to iodine had been obtained. She continued to take iodine for ten months after discharge and lost 35 pounds in weight. After readmission to the hospital, where iodine was withheld for three weeks, she failed to respond when it was readministered. The patient died on the operating table. Microscopically, the thyroid gland showed "diffuse hyperplasia with iodine involution," and in addition, a diagnosis of acute rheumatic fever was made at autopsy. This case is an example of the recognized clinical phenomenon that surgery is safest when it follows iodine therapy given patients for the first time, or when such patients have been untreated by iodine for at least six to eight weeks before operation.

A comparison of these results with those reported from other institutions is of interest. Mortality statistics in thyroidectomy for Graves's disease vary greatly, ranging as high as 13.1 per cent, as reported by Thompson, Taylor, and Meyer[5] at the Cook County Hospital. Maes, Boyce, and McFetridge[6] reported a mortality of 10.6 per cent at Charity Hospital in New Orleans. Among the lowest figures is that of 0.63 per cent given by Clute.[7] It appears that the surgical mortality in Graves's disease at the Peter Bent Brigham Hospital (2.7 per cent) is in the lower range for hospitals in which general surgery is practiced.

A final compilation may be made by a division of the cases into two groups — those with satisfactory and those with poor results.

To the 80 patients who experienced a return to complete good health may be added the 18 patients with hypothyroidism, since all ultimately became asymptomatic through the use of thyroid. In addition, the persistence of exophthalmos should not be considered a poor result, and 10 patients in whom this occurred as a single complication can be added to those with satisfactory results. The seriousness of unilateral vocal-cord paralysis is probably best evaluated in terms of the subsequent course. In 3 patients this occurred as a single complication, and because the later course was quite satisfactory, they can also be added to those with acceptable results. This number can also be supplemented by 2 patients who had temporary tetany. Thus, 113 patients, or 87 per cent, of the 130 followed for a minimum of six months are considered to have had a satisfactory outcome.

The 11 patients who suffered a recurrence or persistence of thyrotoxicosis, the 1 with permanent parathyroprivia, and 1 of those with vocal-cord paralysis should be regarded as having had unfavorable results. The case of vocal-cord paralysis is so classified because a unilateral injury occurred during the first stage of an intended two-stage procedure, and the patient refused further treatment because of this complication. In addition to these complications among the 149 patients subjected to operation, 4 deaths occurred. Thus, unsatisfactory results were obtained in 17, or 13 per cent, of the 130 cases that were adequately followed.

The data in the surgical treatment of Graves's disease (Table 1) indicate that 113 of the 130 patients followed are known to have had results that permitted a return to a normal life, and 13 had complications of some severity, mostly permanent in nature. Four patients did not survive the operation. Nineteen patients did not keep in touch with the hospital, so that a complete history of their cases is not a matter of record. It is also realized that a

TABLE 1. *Results of Surgical Treatment in 130 Cases of Graves's Disease.*

RESULT	PERCENTAGE	
Satisfactory:		
Return to good health	61.5	
Hypothyroidism (single complication)	13.9	
Exophthalmos (single complication)	7.7	
Unilateral temporary vocal cord paralysis (single complication)	2.3	
Temporary tetany	1.5	
Total		87
Unsatisfactory:		
Persistent or recurrent thyrotoxicosis	8.5	
Permanent parathyroprivia	0.8	
Vocal cord paralysis at first-stage operation	0.8	
Death	3.1	
Total		13

few other recurrences of hyperthyroidism may have developed among the small number of patients whose records covered only six months of the postoperative period.

Although this is a teaching hospital, thyroid surgery is not done by the house staff until late in the training period. In this connection, it may be noted that the incidence of complications in the hands of the house staff was not appreciably different from that of the visiting staff with one important exception. Three of the 4 deaths occurred after operations by members of the house staff, although this group performed less than half the procedures.

Since the end of the period during which this study was made, changes have taken place in the method of caring for patients with Graves's disease — chiefly in the preoperative use of thiouracil, alone or followed by iodine. This use of thiouracil may result in a lowered mortality because complete control of the metabolic evidences of the disease are made possible. It is apparent, however, that this will not appreciably alter such complications of surgery as hypothyroidism, parathyroprivia, vocal-cord paralysis or the persistence or recurrence of the disease. It may further be mentioned that the preoperative use of thiouracil entails the administration of this drug from three to eight weeks, and it is generally recognized that it is in the first nine weeks of treatment that the serious reactions to thiouracil are likeliest to occur.[8] Thus, this form of treatment may subject the patients to most of the hazards of medical therapy and subsequently to those of surgery as well. It therefore seems probable that the results of surgery alone, as herewith recorded, approximate those to be expected with the preoperative use of thiouracil.

It is hoped that these figures will help to define the efficacy that medical treatment must achieve if it is to replace surgery in the therapy of Graves's disease. That such a definition is necessary may readily be demonstrated. Although much has been written about the surgical treatment of this disorder, few authors have described the exact postoperative status of their patients. Thus, Frazier and Mosser,[9] describing the end results from the surgical treatment of hyperthyroidism, fail even to mention hypothyroidism, nerve injuries or parathyroprivia. Possibly, this lack of scrutiny was fostered by the absence at that time of a satisfactory alternate method of treatment.

Summary

A review of the records of 149 patients surgically treated for Graves's disease at the Peter Bent Brigham Hospital from 1933 to 1940 showed that satisfactory results were obtained in 113 cases. Persistent or recurrent thyrotoxicosis, lasting parathyroprivic tetany or serious vocal-cord paralysis followed operation in 13 cases, and 4 patients died. The records in 19 cases were incomplete for a minimum of six months following operation.

References

1. Astwood, E. B. Treatment of hyperthyroidism with thiourea and thiouracil. *J. A. M. A.* **122**:78-81, 1943.
2. Thompson, W. O., Morris, A. E., and Thompson, P. K. Thyrotoxicosis following subtotal thyroidectomy for exophthalmic goiter. *Arch. Int. Med.* **46**:946-978, 1930.
3. Thompson, W. O., and Preston, F. W. Persistence and recurrence of toxic goiter following subtotal thyroidectomy. *West. J. Surg.* **49**: 365, 1941.
4. Fulton, M. N., Schnitker, M. A., and Cutler, E. C. Recurrent and persistent thyrotoxicosis following thyroidectomy. *West. J. Surg.* **46**:619-627, 1938.
5. Thompson, W. O., Taylor, S. C. G., III, and Meyer, K. A. Factors influencing operative mortality in exophthalmic goiter. *Ann. Int. Med.* **8**:350-359, 1934.
6. Maes, U., Boyce, F. F., and McFetridge, E. M. Clinical problems of thyroid disease in non-endemic area. *Am. J. Surg.* **24**:232-257, 1934.
7. Clute, H. M. Operative mortality in goitre. *New Eng. J. Med.* **206**: 1240-1243, 1932.
8. Van Winkle, W., Hardy, S. M., Hazel, G. R., Hines, D. C., Newcomer, H. S., Sharp, E. A., and Sisk, W. N. Clinical toxicity of thiouracil: survey of 5,745 cases. *J. A. M. A.* **130**:343-347, 1946.
9. Frazier, C. H., and Mosser, W. B. End results from surgical treatment of hyperthyroidism. *J. A. M. A.* **90**:657-659, 1928.

INFANTILE CORTICAL HYPEROSTOSES*

Report of a Case

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CAFFEY and Silverman,[1] in July, 1945, published the following description of a new syndrome entitled "infantile cortical hyperostoses":

> The principal features of the disorder include: onset in the early part of the first year; tender swellings in one or more of these sites — face and jaws, scapular regions and extremities; and multiple scattered hyperostoses demonstrated roentgenographically in bones adjacent to the tender swellings and also in several other bones whose overlying soft tissues appear to be normal, clinically and roentgenographically. . . . Biopsies of the affected bones in 3 cases showed only hyperplasia of the lamellar cortical bone.
>
> Fever was noted to have occurred in 3 cases. In 1 case there was hyperirritability, and in 1 a blood count disclosed a moderately severe anemia. In all cases the swelling over the site of involvement tended to progress rapidly and to regress slowly.

FIGURE 1. *Photograph of Patient.*
Note the typical facies produced by bilateral swelling of the mandible.

Scurvy and syphilis were definitely ruled out. Infection, however, was not so satisfactorily excluded. Bacterial infection was not proved in any case. Virus infection or an allergic reaction was considered as a possible cause of the disorder.

Smyth et al.[2] recently published an article relating to a condition occurring in infants and sometimes in older children characterized by irritability, fever, anemia with leukocytosis and a periosteal reaction of various bones. They reported 7 cases in which the most constant observation was a varying degree of periosteal reaction producing new bone and giving a laminated, onion-peel appearance. Biopsies of the affected bones and routine studies were of no aid in ascertaining the etiology of the condition. Biopsies of the affected muscles in 2 cases, however, showed evidence of dystrophy suggesting a metabolic factor. Sulfadiazine and a high vitamin C intake did not affect the course of the disease. Penicillin was not tried. All the patients survived, most of the cases clearing completely.

FIGURE 2. *Lateral Oblique Projection of the Left Mandible. This film shows the diffuse thickening and the irregular contour of the inferior border.*

The following case showed clinical manifestations and x-ray findings similar to those reported in the two papers cited above.

A. L., a 3-month-old boy, was admitted to the Charles V. Chapin Hospital on April 24, 1946, with a questionable diag-

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nosis of parotitis. The weight at birth had been 8 pounds, 4 ounces, and the birth was stated to have been normal. A slight fever of unknown etiology during the first week of life passed away without sequelae. Bottle feedings of an evaporated-milk formula were taken well, and orange juice and cod-liver oil in adequate amounts were started at 1 month of age. The mother and father were living and well, as were eight siblings. The patient had received no vaccination or immunization.

About 10 days before admission, the mother had noted that the child was irritable and cried whenever he was touched around the right side of the face. No fever was noted at that time. An actual swelling around the right parotid region was noted by the mother about 1 week prior to admission, was

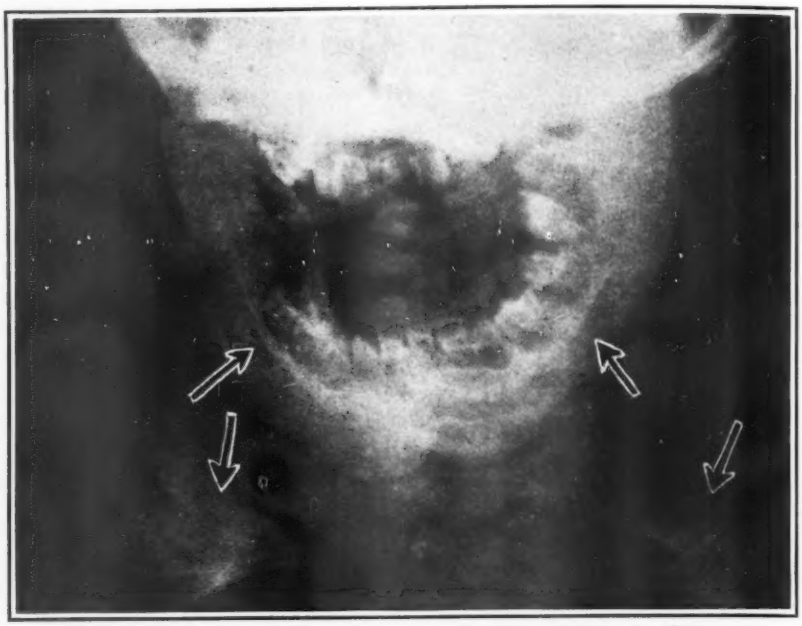

FIGURE 3. *Anteroposterior Projection of the Jaw.*
This film shows the thickened areas of bony involvement. The arrows point to the hyperostotic regions of the mandible and clavicles.

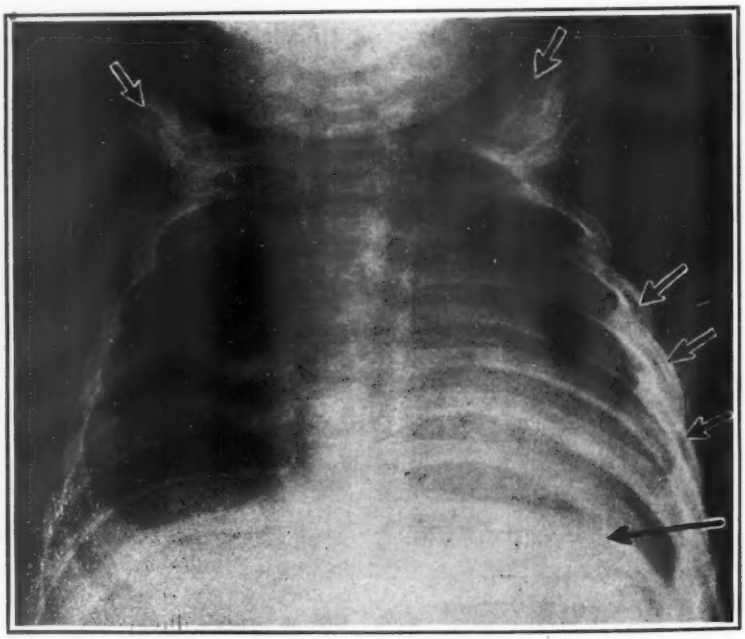

FIGURE 4. *Anteroposterior Projection of the Thorax.*
This film shows the hyperostotic involvement of both clavicles and the anterior and axillary portions of the ribs indicated by arrows.

observed to be rapidly enlarging. During that time the child took his food fairly well but vomited occasionally.

Physical examination disclosed a well developed and well nourished but slightly pale infant. In the right parotid region there was a rather firm, nonred swelling that seemed to be attached to the ramus of the jaw (Fig. 1). Palpation of this area caused the child to cry. The mouth showed no signs of disease.

Examination of the blood revealed a red-cell count of 4,780,000, with a hemoglobin of 68 per cent, and a white-cell count of 24,000. Nineteen days later the white-cell count was 29,800, with 40 per cent neutrophils, 47 per cent lymphocytes, 9 per cent monocytes, 3 per cent eosinophils and 1 per cent basophils. Examination of the urine showed an occasional granular cast and an occasional white cell per high-power field in the sediment on several specimens. Nose and throat cultures were negative for diphtheria bacilli and hemolytic streptococci. The spinal-fluid findings were normal. A blood culture was sterile after 7 days' incubation. Tuberculin and blood Wassermann reactions were negative. The serum calcium was 9.7 mg., and the serum phosphorus 5.4 mg. per 100 cc.

X-ray films of the jaws, skull and the entire skeleton were not revealing, and at that time the diagnosis was thought to be mainly confined to a lesion in the parotid gland. The second set of plates, taken about 3 weeks after admission, revealed definite changes in the mandible; the differential diagnosis varied between an infectious process, osteomyelitis and sarcoma.

The diagnosis of infantile cortical hyperostoses was then entertained, and the plates (those taken before May 26) and a copy of the clinical abstract were sent to Dr. John Caffey, who confirmed the diagnosis and interpreted the plates as follows:

> Cortical hyperostoses are visualized in several sites of the skeleton. There is a massive mandibular hyperostosis confined to the right side of this bone, which thickens the body, ramus, coronoid process and articular process. In the calvarium external hyperostoses of both parietal bones can be demonstrated in the film of May 7, 1946. In a later film of the thorax, a massive cortical thickening of the right clavicle is seen. The remainder of the skeleton is normal roentgenographically. There are no signs of scurvy, syphilis or rickets.

The patient continued to run an intermittent fever, the temperature going as high as 102.5°F., and continued to be irritable. During his first stay in the hospital, he received a total of 2,400,000 units of penicillin intramuscularly and at another time received 10 gm. of sulfadiazine. Neither of these agents altered the course of the disease.

The swelling in the right side of the face continued to enlarge, and about 2 weeks after admission a 4-cm., raised, red area that at first seemed soft appeared in the right occipitoparietal region. This mass was needled, and a culture of the solid material obtained grew out a few colonies of *Staphylococcus albus* and a rare one of *Staphylococcus aureus*. This was followed by the appearance of a similar mass on the left side of the head.

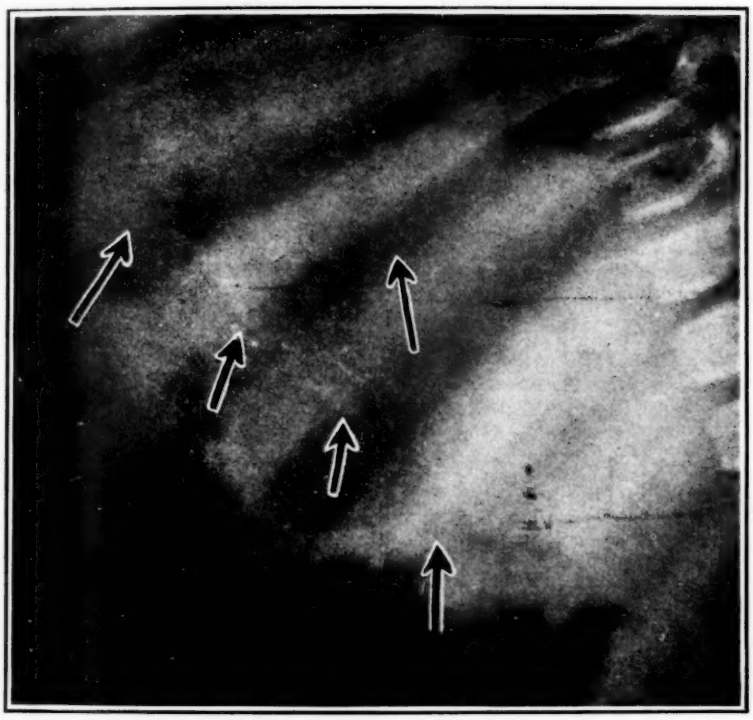

FIGURE 5. *Lateral Projection of the Lower Left Ribs.*
This film shows thickening and broadening of those areas indicated by the arrows.

About 1 month after admission, following a transfusion, examination of the blood showed a red-cell count of 4,330,000, with a hemoglobin of 76 per cent, and a white-cell count of 18,550. The differential was relatively unchanged. The white-cell count on June 20 was 36,450, with 34 per cent neutrophils, 63 per cent lymphocytes and 3 per cent monocytes.

On May 29, the patient was transferred to the Rhode Island Hospital for further treatment. On the morning of transfer a painful reddish swelling was noted in the region of the right sternoclavicular junction. The following is a detailed x-ray report from the Rhode Island Hospital on films taken on June 8:

> *Skull.* The calvarium is not enlarged. In the posterior parietal region and in the posterior portions of the occipital bone, there are several scattered patches of thickening of both the internal and external plates, together with small

areas of punctuate decalcification. One of these areas corresponds to the region of soft-tissue prominence in the right side. The soft-tissue prominence on the left side does not correspond to a similar area. No other definite productive or destructive bone lesion is seen elsewhere in the skull. There is no diastasis of the sutures.

Mandible. The entire mandible shows a diffuse general enlargement, with a somewhat lobulated inferior border (Figs. 2 and 3). On both sides the limits of the original bony mandible can be distinguished, together with the additional layers of fairly solid bony substance. The outlines are smooth. No destructive areas are visible.

Clavicles. The left clavicle shows a large spindle-shaped mass of bony material surrounding somewhat more than the lateral half of the bone chiefly along the upper surface (Figs. 3 and 4). The bony mass is uniform and also shows a slight lobulation in places. No destruction of the original clavicle can be seen. The right clavicle shows a more advanced stage of apparently the same process (Figs. 3 and 4). Here, the additional bony accretion is also along the upper surface, where there is likewise a definite, lobulated peripheral outline.

Spine. The cervical, thoracic and lumbar spine shows a normal alignment and no definite productive or destructive bony lesion. There are no definite congenital anomalies.

Ribs. On the left side the 3rd, 4th and 5th ribs show zones of similar bony deposits along the axillary portions (Figs. 4 and 5). The inner surfaces of these bones are projected in two areas along the lateral costal wall, resembling lines of pleural exudate. Similar appearances are also seen along the anterior portions of the 9th, 10th and 11th ribs on both sides.

Pelvis. No definite bony abnormalities are observed in the pelvic bones. Both hip joints show normal development for the patient's age.

Long bones. The examination includes both humeri and the entire lower extremities on both sides. No definite productive or destructive bony lesion is noted in any of the bones.

Conclusions. The appearances are consistent with those found in a newly described syndrome, which has been called "infantile cortical hyperostoses."

On return to this hospital about 2 weeks later, the clavicles were both enlarged; they were not red but were slightly tender to palpation. The two swellings on the head had decreased in size but were still firm and slightly red. The swelling on the right side of the head had broken down. The right jaw looked larger, and with a finger inside the baby's mouth and one outside, the bony reaction was palpable between the fingers. On June 22 the left jaw became involved in a process similar to that involving the right on admission. The left half of the mandible was larger than the right.

The clinical features, laboratory data and x-ray findings of this case conformed with the material gleaned from the cases presented by Caffey and Silverman[1] and Smyth et al.[2] The main features were hyperirritability, fever, leukocytosis and anemia. The x-ray films of the mandible, clavicles and certain ribs showed the typical reaction described by one author as a periosteal reaction[2] and by another author as hyperostosis of the cortices.[1]

This case was unique in the fact that there was involvement of the skull and bones of the calvarium.[3]

It is remarkable that these lesions develop so rapidly and regress so slowly, but if this patient follows the clinical course of those in previous cases of this kind, the prognosis is good.

Summary

A case of infantile cortical hyperostoses is presented. Penicillin and sulfadiazine proved to be of no value in the treatment of the patient.

References

1. Caffey, J., and Silverman, W. A. Infantile cortical hyperostoses: preliminary report on new syndrome. *Am. J. Roentgenol.* **54**:1-16, 1945.
2. Smyth, F. S., Potter, A., and Silverman, W. Periosteal reaction, fever and irritability in young infants: new syndrome? *Am. J. Dis. Child.* **71**:333-350, 1946.
3. Caffey, J. Personal communication.

MEDICAL PROGRESS

SYPHILIS

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WITH the termination of World War II and the return of several million young men to civilian life, the program for the control of syphilis is faced with a great problem. In spite of the lowest wartime venereal-disease rates for any nation in history, it is exceedingly important that consistent effort be maintained to eradicate syphilis. Even extremely efficient military supervision at separation centers cannot prevent the release of some cases of uncontrolled fresh infection. The cessation of large-scale effort by the armed forces requires increased public-health activity. Plans for the future in this respect, in addition to the continued study of newer methods of therapy, constitute the most significant phases of the problem of syphilis at present.

Public Health

The most widespread case-finding program ever attempted was introduced by Selective Service before the United States entered the war. Protection of the armed forces from infection was greatly furthered by intensive contact-tracing measures instituted by the United States Public Health Service and local health departments. Most of the burden of this work now falls to civilian health authorities in the face of an increasing number of young men returning to civilian life. A great deal of careful planning for further procedures is required. Lacking the uniformity of military control, the Nation must return to the enforcement of laws and regulations by each community. It has been pointed out that a loose legal framework is now in use in many states for control of the venereal diseases.[1] Existing laws and regulations are for the most part merely adaptations of those designed for the control of other infectious diseases. Since each contagious disease presents unique problems, the application of such laws to any one type of infection cannot be expected to give the best possible results. As the laws stand, the principles of individual civil liberty are not always sufficiently protected. Health departments guarding the public against venereal disease ought not to depend wholly on law-enforcement machinery. Coercive methods should be used only as a last resort in the exceptional patient who is infectious and proves refractory to all methods of persuasion. It may seem hopeless in some cases to obtain co-operation through persuasion and education, but experienced workers in this field find that it can be done in all except a few cases. When rapport can be established with such a recalcitrant patient, it is usually productive of far greater and more lasting co-operation. Resorting to enforcement of regulations by police officers often results in still greater antagonism.

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Incidence of Syphilis

A survey of 5000 military inductees who were suspected of having syphilis showed that 570 (11.4 per cent) were proved to be completely free of the disease.[2] Most of these cases were included on the basis of a single positive blood test. There was considerable doubt concerning the diagnosis in an additional 6.3 per cent, and another 10.6 per cent were probably cured of the infection. Thus, only slightly more than 70 per cent of the original 5000 suspected cases were shown to have syphilis that required attention. Nearly 60 per cent of the patients in this group had not been treated and had had previously unrecognized infections. This emphasizes the great ease with which syphilis may spread unobserved through the general population and probably through the hands of many practicing physicians. In all, the blood serologic tests for syphilis of the Selective Service disclosed more than 700,000 cases.[3]

A study of venereal-disease rates in the Army after the termination of fighting in various theaters of operation revealed a sharp rise in the incidence of infections.[4] These data included both the war areas and the United States itself. The relaxation of military discipline, compulsory educational procedures, provision of prophylaxis and treatment of infected military personnel, as well as the resultant loss of contact information, will sharply increase the burden on civilian health authorities. Although separation centers examined all soldiers for evidence of venereal disease within forty-eight hours of release and treated those with infection, many early cases doubtless slipped through during the stage when a diagnosis was impossible. The United States Public Health Service received reports on all infected soldiers requiring follow-up care and in turn notified the appropriate state health departments regarding the need for further diagnostic

procedures or treatment. It was the opinion of military authorities that the educational program represented one of the most important features in the control of venereal disease.[5] This fact should be recognized by all public-health authorities and carried over into civilian life.

The incidence of syphilis in the United States showed a decrease from 1944 to 1945. Syphilis reported for the first time for the calendar year 1944 in the United States numbered 398,907 cases.[6] This figure dropped to 335,586 cases reported for the first time in 1945.[7] This represents a reduction of almost 16 per cent but concerns only the cases of syphilis discovered during that period. The new infections (primary and secondary cases) were found to have occurred in almost identical numbers. This indicates that up to the end of 1945, the incidence of new cases of syphilis in the civilian population had not been influenced by the return of military personnel.

Control Measures

A second report on Alabama's legally required blood-testing program for syphilis on all persons between the ages of fourteen and fifty years is now available.[8] The ninth county in which universal blood testing has been tried included the first predominantly urban group; this is the most populous county in the state and contains the largest city. The experience gained in mass blood testing in eight previous counties had established basic operating procedures and determined methods for ensuring public respect. The program was carried out by highly trained units designed to carry all publicity and establish primary blood-testing stations, auxiliary laboratories, records and statistics, record and reviewing personnel, physician and telephone follow-up service, personal interview and letter-writing follow-up service, secondary operational centers and a rapid-treatment center. This setup had been found to work with exceptional facility, and during a forty-two day period, 271,775 people were actually blood tested. On the first report, 41,072 persons were shown to have either a doubtful, positive or unsatisfactory serologic test for syphilis; only 32,655 had, by the time of publication, been proved to have syphilis. There were 765 patients with primary and secondary syphilis. This incidence of early syphilis was twelve times that normally reported to the health department during a comparable period. The number of infections brought under treatment could not have been accomplished in years of routine health-department work. Such a program of mass blood testing with follow-up study and immediate treatment, when properly publicized, could not but remove much early syphilis from any community. The cost is relatively low when the testing is done on such a large scale. The full value of these public-health measures is difficult to estimate. It should be pointed out that such a gain against syphilis could be permanently held only if the program were continued at regular intervals. The repetition of such surveys for the group from fourteen to thirty-five years of age seems especially important. Alabama should receive great credit for the institution of such measures on a state-wide basis, and this program may well serve as a model for future efforts by others. A similar campaign has been reported from San Antonio, Texas.[9] Such measures should at least accomplish extensive health education, and even if that were the most noteworthy achievement, the effort would still be distinctly worth while. The importance of the preliminary publicity and education of the public that precede mass surveys cannot be overemphasized. In San Francisco a well conceived educational and case-finding program has been instituted in the industrial field.[10] Educational efforts were directed toward labor groups, and after education of the union heads, the campaign went well. An appreciation of public-health services was fostered among industrial leaders, and with the confidence of both labor and management, the public-health service was able to function smoothly. This illustrates how special groups can be approached to create public awareness of the health, welfare and moral aspects of venereal-disease control.

The value of contact tracing with all new infections cannot be too heavily stressed. An excellent example of how much early syphilis can thus be tracked down may be seen in the story of a small outbreak of early syphilis in western New York.[11] Five patients with early cases divulged the names of 25 persons as contacts, and it was possible to locate 23 of these. Nineteen were found to be infected, and all cases but one were of recent origin. Eight of the infected contacts might have failed to see a physician except for the contact investigations. Prompt reporting by private physicians of all cases and intensive epidemiologic investigation can be expected to bring to treatment many patients with early infectious syphilis who would otherwise go untreated and continue to spread infection. Public-health measures are vital, but there is no practicing physician anywhere who cannot contribute valuable assistance by personal effort in contact follow-up procedures.

Hospitals are an aid in case-finding when routine serologic tests for syphilis are performed on every admission. Many thousands of new cases have been discovered by this means, and the procedure should be strongly urged in all hospitals in which such tests are not at present done. Hospitals will play an increasingly important role in the control of syphilis owing to the advent of penicillin. Nearly 100 per cent of all patients with syphilis could complete the required amount of treatment in a short period if institutionalized. This is too great a burden for present hospital facilities but is a worthy goal, in view of the comparatively small percentage of pa-

tients who completed proper therapy by the older routine methods.

The control of commercialized prostitution was relaxed somewhat after the termination of wartime measures.[12] The United States Public Health Service and the American Social Hygiene Association are exerting every effort to continue this important phase of the control of syphilis. Hawaii has had a particularly severe problem in this respect,[13] and the control of prostitution instituted during World War II resulted not only in a drop in venereal-disease rates but also in fewer sex crimes.[14]

Mortality Rates

A study of the compilation of data by the Bureau of the Census relating to mortality attributable to syphilis reveals interesting material.[15] Since 1939 there has been a steady and appreciable decline in deaths due to syphilis, every region of the country contributing to the lowered rates. Even in the South, where the highest incidence occurs, there has been a distinct decrease in mortality. The most marked decline in death rates for syphilis is for infants under one year of age. The rate in the United States as a whole in 1943 was less than one third that in 1933. The mortality rates for paresis have remained practically stationary in recent years. A study of mortality of untreated syphilis in the male Negro indicates that the untreated disease probably reduces the span of life by about 20 per cent.[16] A group of 410 Negroes were followed over a period of twelve years to determine this fact. A control series consisted of a comparable age group of 201 uninfected Negroes. A large proportion of those who died during the time of observation were examined post mortem. The effect of the treatment of acquired syphilis on life expectancy has been estimated by a study of admissions to the University of Virginia Hospital over a twenty-year period,[17] including 2908 patients; among these patients 202 deaths were reported. Mortality data for the general population from the Virginia State Department of Health supplied control figures. Some patients were followed for as long as twenty years, and the average period of observation was four years. All causes of death were included in computing life expectancy. It was demonstrated that there were highly significant differences between the life expectancy of patients with syphilis and that of the general population, which in that area is unusually stable so that the fluctuation in statistics caused by transients was at a minimum. The syphilitic population under investigation was a treated group, owing to an intensive control program carried out over a long period of years. It was demonstrated that the life expectancy among the syphilitic group was reduced from 10 to 12 per cent below that of the general population. Since the amount of treatment received by these patients is not specified, no estimate can be made of the amount necessary to counteract the influence of syphilis on life expectancy. A comparison of these figures with the 20 per cent decrease in life expectancy among untreated cases[16] indicates that the antisyphilitic therapy prolongs life. Treatment should thus be effective in reducing mortality specifically due to syphilis and in offsetting to some extent the effect of syphilis in reducing life expectancy.

Schamberg,[18] in a review of the literature bearing on the statistical prognosis of syphilis as based on governmental mortality reports, clinical studies, death and autopsy findings, and life insurance data during the twentieth century, points out that the available evidence indicates that syphilis adversely influences life expectancy only through the effects of its late manifestations in the central nervous and cardiovascular systems. He believes that life-insurance companies may insure, at standard rates, the majority of syphilitic patients applying for insurance with no risk of increased death losses. This is at variance with the preceding reports,[15–17] but it serves to emphasize the value of treatment. The late crippling effects of visceral syphilis can practically always be prevented by adequate therapy instituted before damage has occurred. There is a tendency among many physicians to de-emphasize the benefit of treatment in late asymptomatic syphilis. This may be justifiable only if adequate therapy has been given in the past and the patient is properly followed.

Serologic Problems

The diagnosis of syphilis on the sole basis of serologic tests of the blood is fraught with many hazards. It cannot be overemphasized that such a diagnosis in the absence of any other finding should be made with exceeding care. A clinical evaluation of the results of serologic tests for syphilis in 8000 consecutive cases in a marine hospital[19] is an example of the difficulties that may be encountered. One or more tests performed on admission were positive in 226 cases (2.9 per cent). Among these it was eventually decided that 16.8 per cent of cases had false-positive reactions due to upper respiratory infections, virus pneumonia, malaria, smallpox vaccination, scarlet fever, leprosy, balanitis, diabetes, jaundice, infectious mononucleosis, bone tuberculosis and pulmonary tuberculosis. There were only 2 cases in which the so-called "general biologic reaction" was considered to account for a false-positive test. Few patients with what were considered to be false-negative reactions were subsequently found to be syphilitic. The standard qualitative simplified Kolmer–Wassermann tests were employed throughout, each positive test being repeated at least once. The Kahn test is reported to have given a higher incidence of false-positive reactions. It was concluded that the use of only one standard test may miss as high as 16 per cent of cases. It should be emphasized that doubtful serologic tests for syphilis

should not be regarded as insignificant any more than they can be used as direct evidence of syphilis. Nor can a negative report be overlooked in the face of clinical evidence. The value of more than one test for syphilis, as well as the employment of different types of reactions, is further emphasized by the fact that some procedures give lower percentages of false-positive reactions under different circumstances.[20] The Hinton test, for example, shows a lower incidence of such reactions in malaria. Upper respiratory infections and immunization procedures produce fewer false-positive reactions with the Kolmer type of complement-fixation test. Temporary variations in the seroglobulins may give rise to temporary false-positive tests for syphilis. In the vast majority of cases, false-positive reactions are of low titer and usually disappear within a comparatively short time. The possibility of technical errors must always be kept in mind. The diagnosis of syphilis on the basis of blood serologic tests alone may be so complicated as to require repetition of the tests for weeks or months, as indicated in each case. A rather complete summary of this problem, presented in readable form by Kampmeier,[21] merits the consideration of anyone faced with such a diagnostic dilemma.

There are continued attempts to refine the technics and to develop new methods designed to eliminate nonspecificity in the blood serologic tests for syphilis. Kahn[22] reports on the use of the so-called "zone reactions" — a serologic method based on the use of multiple serum-antigen ratios that is mainly useful in known or suspected cases of syphilis in which serodiagnostic tests give what are suspected of being false-negative results. Kahn also believes that the procedure provides a better criterion of cure than negative results by standard tests. Rein and Elsberg[23] have published a critical dissertation on the practical value of current verification tests in the serodiagnosis of syphilis. Six methods were considered that have been described for the differentiation of the true-positive from the false-positive serologic reactions for syphilis. It is the opinion of these authors that none of the verification procedures have been able to distinguish consistently between true-positive and false-positive tests. This belief, shared by a number of other serologists, in addition to the impracticability of verification tests in most laboratories, has limited the use of such procedures to large institutions where research facilities are available. Microflocculation tests for syphilis using cardiolipin antigens have recently been described.[24, 25] It is claimed that a comparison of the test results by these technics with those by other methods indicates a satisfactory level of sensitivity and specificity. There is some belief that cardiolipin antigens may prove more sensitive than those previously employed. Quantitative serologic tests continue to be used for special diagnostic problems.[26] These are also impractical for routine application because of the larger amount of serum required and the higher degree of technical skill involved. It is possible to follow the serologic trend in various phases of syphilis under treatment with such quantitative tests, which are of great value in estimating the effectiveness of treatment in early syphilis. The application of these principles to various phases of syphilis has recently been discussed.[27]

False-Positive Reactions

A careful survey was undertaken by the syphilis division of the Johns Hopkins Hospital[28] to determine whether positive blood serologic tests for syphilis may be differentiated from reactions due to other factors by means of serologic methods at present available. Serums were obtained from known cases of syphilis, from patients having biologic false-positive tests, from cases of undetermined status, from a normal group and from cows and horses. Specimens were shipped to various laboratories for the performance of numerous serologic tests, including several special technics. According to this study, there is no "serologic pattern" that will differentiate true from false reactions or one type of syphilitic infection from another. Apparently, no single test or combination of tests was found capable of diagnosing true from false positivity by examination of a single specimen of serum. Until new serologic methods can be developed, differential diagnosis between syphilis and other reagin-producing diseases must continue to be made by clinical examination and by serial quantitative serologic tests repeated over periods of days to years. The frequent warning regarding clinical study of each case[29] and attempts to rule out causes for false-positive reactions[30] are to be found in practically every article dealing with this problem. Varicella is one of the more recently described possible causes of false-positive serologic tests for syphilis.[31] Lymphogranuloma venereum has likewise been added to the list.[32] The influence of malaria on the serologic tests for syphilis continues to be studied.[33] Apparently, there is no relation between the degree of temperature in malaria patients and the number of false-positive reactions. There is also no apparent correlation between the number of attacks of malaria and the development of positive serologic reactions for syphilis, nor has this disease been proved to produce any change in the spinal fluid.[34]

The occurrence of false-positive reactions in serologic tests for syphilis following repeated blood donations has received considerable study. Stokes et al.[35] reviewed the findings among specimens collected from 210,261 Red Cross blood donors over a nine-month period, 489 of which gave definite positive reactions to serologic tests for syphilis. Of these, 79 subjects were selected for intensive follow-up and evaluation; 40.5 per cent were finally adjudged to have syphilis. After exhaustive clinical

and laboratory studies, it was necessary in most cases to establish the diagnosis on the basis of serologic findings. Elaborate batteries of tests evaluated according to a special classification procedure proved to be the most satisfactory method of studying the material. Many borderline cases were extremely difficult to decide. One might envision the possibility that it could become too easy to give treatment in doubtful cases when penicillin therapy is developed to the point of greater facility of application. Another report covers the observation of 300 healthy seronegative reformatory inmates who gave blood donations.[36] Almost 10 per cent of these donors developed some degree of seropositivity, which reverted to negativity in eight weeks. The serums of these patients were subjected to repeated tests for syphilis by six serodiagnostic technics. A second report from multiple donors observed at the American Red Cross Blood Donor Service[37] indicated that there is a tendency for positive serologic reactions to diminish rather than to increase with multiple donations.

Seroresistance

An unusual article by Moore,[38] which is worth reading by anyone who treats syphilis, presents a discussion of the problem of seroresistance (so-called "Wassermann fastness") in syphilis, primarily to guide the physician in discussing this matter with his patient. The difficulties encountered in attempting to explain such situations to even the most intelligent person are graphically portrayed, and simple explanatory devices outlined. The reasons for giving treatment even when no physical evidence of syphilis exists and no history of the disease is obtained are shown. The value of yearly physical examinations and semiannual tests of the blood are pointed out. This paper answers many questions that frequently confront both the physician in general practice and the specialist dealing with syphilis.

Clinical Problems

With the bulk of emphasis in current literature dwelling on various phases of penicillin therapy and public-health problems, there have been fewer reports than usual on the everyday clinical problems in the management of syphilis. A few articles nevertheless merit consideration.

Beerman[39] has presented an instructive survey of reinoculation of human beings with *Treponema pallidum*. He points out that the introduction of each new curative agent or method of therapy is accompanied by increased reports of reinfection. Beerman believes that part of this may be a reluctance on the part of the supporters of a new therapy to accept the possibility of relapse. After a complete and extensive review of the literature, it is pointed out that reinoculation with *T. pallidum* can be successful in all phases of untreated human syphilis (superinfection). The reinoculation lesions resemble those representing the phase of the patient's syphilis at the time of reinoculation. Beerman believes that reinoculation of patients supposedly "cured" of syphilis (reinfection) rarely occurs. He does not consider the data on reinoculation of human beings with syphilis sufficient to answer definitely the question whether reinfection is possible in man. Although there may be some justification in the claim that foreshortened treatment schedules prevent the development of immunity, the data available cannot be construed as a rational basis for the voluminous number of cases of reinfection reported in patients treated by intensive therapy. It must be remembered, however, that there are no absolute criteria of biologic cure or adequate means of identifying asymptomatic infections in man, and it is possible that reinfections may take place on a scale larger than hitherto suspected. In this connection, it is interesting to note the report of a chancre developing in a patient with cardiovascular syphilis.[40] The patient had had adequate therapy for syphilis, and the serologic tests had been negative for several years. The syphilitic cardiovascular disease had apparently been arrested. Such a case presents a nice problem of reinfection versus superinfection.

The occurrence and significance of fever in syphilis have received little attention, since succeeding generations appear to offer milder clinical manifestations of the disease. Wallman[41] has reviewed the significance of fever in syphilis. He points out that it may occur in the secondary phase of the disease and is occasionally observed in early syphilis without eruption; an intermittent fever can occur and may be confused with malaria. A moderate temperature accompanied by generalized muscle pain and gastric disturbance is occasionally found. There are also completely irregular patterns. Hypopyrexia may also occur in either acquired or congenital syphilis. Pyrexial activations during therapy are discussed. Thermal reactions may also be seen when latent syphilis becomes activated, whether spontaneously or by physical trauma, intercurrent disease and so forth. Wallman regards thermal reactions occurring during the treatment of syphilis as an index to the resistance of the *T. pallidum* and believes that in such cases the dosage of drugs should be increased or other measures employed.

Jordon and Dolce[42] have recently recorded observations in 169 cases of late syphilis over a period of ten years or more. It was found that there is a decided tendency for the blood serum of the patients who were untreated or poorly treated to fluctuate over a period of years. Consequently, the negative serologic reaction in such cases, even on repeated examination, does not necessarily mean spontaneous serologic cure. Approximately 25 per cent of the untreated or poorly treated patients with latent syphilis became seronegative spontaneously and remained so over a period of years. From 20 to

25 per cent of these patients (massed racial groups, including Negroes) developed some cardiovascular complication when observations were included over a period in excess of thirteen years. It was apparent that a blood serum that tended to fluctuate in degree of positivity indicated a relatively good clinical outcome, whereas the persistence of strongly positive reactions predicted a poor clinical outcome. As a corollary it was found that in patients with adequately treated latent syphilis there was a decided tendency for the blood serums to fluctuate. Frank, early syphilis did not appear to provide immunity to late complications. Adequate antisyphilitic treatment apparently reduces the hazard of late serious complications to a minimum, even though in patients with latent syphilis there was only a 17 per cent increase in long-term serologic reversals, compared to the 25 per cent spontaneous reversals after little or no treatment. In well treated latent syphilis there was no apparent relation between the state of the blood serum and the development of late complications. Arsenical drugs seemed more efficacious than heavy metals in preventing late complications. Twenty to twenty-nine injections of an arsenical drug were regarded as constituting adequate therapy. This should be combined with alternating courses of a heavy metal. More than this amount did not result in a reduction of complications. Forty to sixty injections, or possibly less, of a heavy metal appeared sufficient when combined with the adequate arsenical therapy. Further administration of heavy metal did not reduce the likelihood of late complications. The findings of these observers warrant more than the usual consideration. It has repeatedly been emphasized that prolonged periods of observation are essential to determine the adequacy of any form of therapy for syphilis or to gather adequate data of almost any sort concerning the disease. This is the first series on record of more than 40 patients followed for ten years or more in whom adequate examinations and repeated serologic tests were done. Such work requires time and is painstaking and tedious, but affords invaluable information.

The early diagnosis of cardiovascular syphilis has been stressed by Dressler.[43] A study of 1270 cases of proved syphilis resulted in a diagnosis of cardiovascular syphilis in 30.7 per cent. Seventy-eight of these cardiovascular cases were uncomplicated aortitis. These are comparatively high percentages. Of 128 patients with cardiovascular syphilis who recalled the chancre, a diagnosis of uncomplicated aortitis was made in 38 cases within ten years after the acquisition of infection. Dressler, reviewing his methods of study and criteria for the diagnosis of aortitis, believes that careful study enables one to establish the diagnosis earlier than is usually believed, and states that uncomplicated aortitis can be diagnosed clinically in a patient with an aorta of normal size. It has been claimed that calcification in the ascending aorta is strongly indicative of syphilis.[44] A comparison of the clinical, roentgenologic and pathological findings in 66 autopsied cases of syphilitic aortitis were compared with those in a group of 62 autopsied cases of severe arteriosclerosis of the aorta. Linear calcifications in the ascending portion of the aorta were present on the roentgenograms in 22.7 per cent of the cases of syphilitic aortitis, whereas only 3.2 per cent of the arteriosclerotic group were found to have calcium deposits visible in the ascending aorta. Calcification in this location was considered to surpass the reliability of negative serologic evidence of syphilis. Such calcification was seldom found as an early sign of syphilitic aortitis, occurring most frequently in the older patients with relatively quiescent cases of syphilis. A description has appeared of 5 patients who developed serious syphilitic lesions of the vascular or cardiovascular organs in early adult life.[45] Clinical manifestations of syphilitic heart disease appearing in early decades are comparatively rare. The patients in this group varied from five to thirty-one years of age. The duration of infection in 3 of the cases was known to be two, thirteen and fifteen years. Post-mortem examinations were done in 4 cases.

Headaches after lumbar puncture have been studied in a statistical report by Underwood.[46] Incapacitating attacks occurred in 19 per cent of 500 cases in which punctures were done. Evidence was presented that bed rest following a lumbar puncture does not reduce the incidence of post-puncture reactions. If a severe headache results, however, bed rest for twenty-four to forty-eight hours should be advised. The use of caffeine with sodium benzoate intravenously may be of value in alleviating the discomfort of post-puncture headache if the patient cannot rest. Sedation before the puncture was not found beneficial. Patients presenting emotional reactions to the spinal tap had incapacitating reactions more frequently than calm, quiet persons. As has frequently been observed by others, patients with neurosyphilis had fewer post-puncture attacks than any other group. The problems encountered in the diagnosis of acute syphilitic meningitis were pointed out in a report of 9 cases, 5 of which presented diagnostic difficulties.[47] In 2 cases the symptoms developed while the patient was receiving treatment with bismuth preparations. Since syphilitic meningitis often improves without treatment and since patients with other types of lymphocytic meningitis may get well coincidentally with antisyphilitic treatment, such therapy cannot be considered a diagnostic test. Other difficulties that may be encountered are the occurrence of false-positive Wassermann reactions in the spinal fluids of patients with nonsyphilitic meningitis and occasionally false-negative reactions in patients with syphilitic meningitis. Unless the patient is critically

ill, it seems advisable to withhold antisyphilitic therapy until a definite diagnosis can be established.

Therapy

The use of penicillin in the treatment of syphilis is again considered a separate main division in this progress report.

Intensive Therapy

Shaffer[48] has reviewed two groups of patients with early syphilis treated by separate intensive therapy schedules; 210 patients received a fifteen and two-third weeks' schedule consisting of thirty injections of Mapharsen and eight injections of bismuth. Reactions necessitated the discontinuance of treatment in 7 cases. A second group of 352 patients was placed on an eight-week schedule that included twenty-four injections of Mapharsen and eight injections of bismuth given concurrently. Discontinuance of treatment was necessary in 8 cases. There were no fatal reactions in either group. Shaffer found that the results of treatment were essentially satisfactory in both series, but only among those who followed treatment faithfully. His opinion is that these intensive plans are satisfactory and adaptable to either private practice or clinics, but that case holding presents the greatest problem. A less satisfactory rate of cure was observed in a group of 206 patients with early syphilis, given two injections of Mapharsen daily for a period of six days by other workers.[49]

Several studies of liver function in early syphilis under intensive arsenotherapy have been reported. In one group the tests employed were the blood prothrombin concentration, the serum bilirubin level, the retention of bromsulfalein and the rate of hippuric acid synthesis.[50] Among the 22 patients only 3 were found to have normal liver-function tests prior to treatment, suggesting some degree of syphilitic hepatitis. All cases showed impairment of liver function by one or more tests subsequent to the administration of massive doses of arsenical drugs by the five-day intravenous method. The liver function of all patients returned to normal within six months after the arsenotherapy. This indicates that, although hepatic damage results from arsenotherapy, the injury is not permanent nor is it often sufficient to cause clinically recognizable liver disease. Another series of 49 patients receiving five-day therapy were studied with the following liver-function tests: plasma protein, cephalin flocculation, intravenous hippuric acid and sulfobromophthalein.[51] Approximately 35 per cent showed evidence of liver damage prior to treatment, again indicating active hepatitis during the primary and secondary stages of syphilis. There was no evidence of liver damage in any of these cases subsequent to massive arsenotherapy. Approximately 90 per cent of patients with abnormal tests before treatment exhibited the same or improved liver-function tests following arsenotherapy. These findings suggest that large doses of arsenoxide given within a five-day period do not usually produce detectable liver damage. The disagreement in these two reports[50, 51] may be partially due to the diversity in liver-function tests employed.

The massive five-day to eight-day intravenous drip arsenotherapy of syphilis appears to be sliding further into disfavor. This method was studied over a period of ten years by numerous groups of investigators but never reached universal application because of the technical difficulties involved and the high incidence of serious and fatal reactions. Multiple-syringe programs for varying periods of days and weeks were in the process of being evaluated at the time of the advent of penicillin. Although these schedules showed great promise and fewer untoward effects, penicillin now bids fair to supplant them all. Combinations of penicillin and chemotherapy, as pointed out below, seem to show the greatest promise.

The use of hyperpyrexia in ocular conditions due to syphilis has recently received attention. One group of 35 cases was treated with specific antisyphilitic chemotherapy in conjunction with the use of the Kettering hypertherm.[52] Four of 19 cases of syphilitic atrophy of the optic nerve showed improvement; clinical progression of symptoms was arrested in 7, and the remainder continued to progress. Four of 6 cases of acute syphilitic choroiditis were decidedly improved by this treatment. In 6 cases of acute iritis associated with secondary syphilis excellent therapeutic results were obtained. The therapy was also beneficial in the treatment of interstitial keratitis, with marked alleviation of severe pain and photophobia. A report by Bruetsch[53] from the Johns Hopkins Hospital concerns 250 patients with syphilitic primary optic atrophy treated with malaria. It is pointed out that the pathological basis of syphilitic optic atrophy is more like the process of dementia paralytica than that of tabes. Malaria therapy inhibits the inflammatory element, and the degeneration of the nerve fibers ceases. Since the inflammatory process usually advances from the periphery toward the interior, enough normal tissue of the central portions of the nerve is left for useful vision. For three years following malaria therapy the slow progression of failure of vision may continue. In patients who react favorably to this treatment, however, the constriction of the visual fields will gradually expand, evidencing capacity for recovery of partially damaged nerve fibers.

It has been found that there is some value in the use of electric shock in the treatment of dementia paralytica.[54] This should not be considered a treatment of choice, but regarded as an adjuvant method in cases in which hyperpyrexia, penicillin, chemotherapy and combinations of these may fail.

There has been a belief in some quarters that the

use of inoculation malaria for the treatment of neurosyphilis presented a hazard to other institutionalized patients. A recent survey of this problem indicates that accidental transmission of therapeutic malaria practically never occurs.[55]

(To be concluded)

References

1. Gillis, E. A. Cooperation of health officers and police departments. *J. Ven. Dis. Inform.* **27**:62-64, 1946.
2. Zellermayer, J. Syphilis in inductees: analysis of 5,000 cases. *J. Ven. Dis. Inform.* **26**:194-198, 1945.
3. Heller, J. R., Jr. Venereal disease epidemiology in wartime. *Am. J. Pub. Health* **35**:1210-1216, 1945.
4. Sternberg, T. H., and Howard, E. B. Current Army venereal disease rates. *J. Social Hyg.* **31**:530-533, 1945.
5. Larimore, G. W., and Sternberg, T. H. Does health education prevent venereal disease? Army's experience with 8,000,000 men. *Am. J. Pub. Health* **35**:799-804, 1945.
6. Venereal Disease Division, U. S. Public Health Service. Personal communication.
7. Cases of syphilis and gonorrhea reported for first time in states, territories, and possessions for year 1945. *J. Ven. Dis. Inform.* **27**:112, 1946.
8. Smith, W. H. Y., and Denison, G. A. Blood testing and treatment program in Jefferson County, Alabama. *J. Ven. Dis. Inform.* **27**: 94-103, 1946.
9. Robbins, L. C., and Green, W. S. Preliminary report on San Antonio blood test campaign. *J. Ven. Dis. Inform.* **27**:196-199, 1946.
10. Koch, R. A., Arnstein, L., and Painter, A. C. San Francisco industrial venereal disease educational and case-finding program. *J. Ven. Dis. Inform.* **27**:9-19, 1946.
11. Mattison, B. F., and Harris, E. H. Outbreak of early syphilis in western New York State. *New York State J. Med.* **45**:1105, 1945.
12. Staff, American Social Hygiene Association. War against prostitution must go on: report on current status of commercialized prostitution. *J. Social Hyg.* **31**:500-507, 1945.
13. Allison S. D. Honolulu myth. *J. Social Hyg.* **32**:77-81, 1946.
14. Laune, F. F. Fighting "sin in paradise." *J. Social Hyg.* **32**:67-76, 1946.
15. Usilton, L. J. Mortality trends for syphilis. *J. Ven. Dis. Inform.* **27**:47-52, 1946.
16. Heller, J. R., Jr., and Bruyere, P. T. Untreated syphilis in male Negro. II. Mortality during 12 years of observation. *J. Ven. Dis. Inform.* **27**:34-38, 1946.
17. Smith, D. C., and Bruyere, M. C. Effect of treated acquired syphilis on life expectancy. *J. Ven. Dis. Inform.* **27**:39-46, 1946.
18. Schamberg, I. L. Prognosis of syphilis: critical review of clinical, autopsy, and life insurance studies. *Am. J. Syph., Gonor. & Ven. Dis.* **29**:525-550, 1945.
19. Lubitz, J. M. Clinical evaluation of serologic tests for syphilis in eight thousand cases. *Illinois M. J.* **89**:20-25, 1946.
20. Chargin, L., and Rein, C. R. Reliability of serologic tests for syphilis. *J. Mt. Sinai Hosp.* **12**:111-115, 1945.
21. Kampmeier, R. H. Serodiagnosis in syphilis. *J. Tennessee M. A.* **38**:404-409, 1945.
22. Kahn, R. L. Optimal zone reaction in diagnosis and treatment of syphilis. *Arch. Dermat. & Syph.* **53**:633-642, 1946.
23. Rein, C. R., and Elsberg, E. S. Are current verification tests of practical value in serodiagnosis of syphilis? *J. Invest. Dermat.* **6**:113-127, 1945.
24. Rein, C. R., and Bossak, H. N. Cardiolipin antigens in serodiagnosis of syphilis: microflocculation slide test. *Am. J. Syph., Gonor. & Ven. Dis.* **30**:40-46, 1946.
25. Harris, A., Rosenberg, A. A., and Riedel, L. M. Microflocculation test for syphilis using cardiolipin antigen: preliminary report. *J. Ven. Dis. Inform.* **27**:169-174, 1946.
26. Kile, R. L., and Lund, H. Quantitative serological tests in syphilis. *Bull. Acad. Med. (Cleveland).* (No. 11) **30**:10-24 (November), 1945.
27. Weiner, A. L., and McNamara, M. Practical application of quantitative serologic tests for syphilis. *Ohio State M. J.* **41**:517-520, 1945
28. Scott, V., Rein, C. R., Schamberg, I. L., Moore, J. E., and Eagle, H. Serologic differentiation of syphilitic and false positive sera. *Am. J. Syph., Gonor. & Ven. Dis.* **29**:505-528, 1945.
29. Heyman, A. Biologic false positive serologic tests for syphilis. *J. M. A. Georgia* **34**:165-167, 1945.
30. Page, S. G., Jr., and Heimoff, L. L. Biologic false positive serologic tests for syphilis: study of 100 cases. *Virginia M. Monthly* **73**: 153-159, 1946.
31. Kane, L. W., and Henneman, P. H. False-positive Hinton reactions following chicken pox. *New Eng. J. Med.* **233**:407-409, 1945.
32. Heyman, A., and Webb, E. L. False positive serologic reactions for syphilis in lymphogranuloma venereum. *J. Ven. Dis. Inform.* **27**: 122-126, 1946.
33. Cox, C. B., and Durant, M. J. Influence of malaria on Kline and complement fixation (Wassermann) tests for syphilis. *M. J. Australia* **1**:320-325, 1945.
34. Robinson, H. M., Jr., and McKinney, W. W. Effect of vivax malaria on spinal fluid and blood serologic test for syphilis. *J. A. M. A.* **129**:667, 1945.
35. Stokes, J. H., Boerner, F., Hitchens, A. P., and Nemser, S. Nonspecific reactions in routine blood testing for syphilis. *J. A. M. A.* **130**:57-60, 1946.
36. Barnard, R. D., Rein, C. R., and Doan, C. A. False positive serologic tests for syphilis following blood donation. *Am. J. Syph., Gonor. & Ven. Dis.* **30**:255-263, 1946.
37. Boynton, M. H. Incidence of positive serologic reactions in multiple blood donors. *Am. J. Syph. & Ven. Dis.* **30**:252-254, 1946.
38. Moore, J. E. Seroresistance (Wassermann-fastness) in syphilis: discussion for patient. *Am. J. Syph., Gonor. & Ven. Dis.* **30**:125-133, 1946.
39. Beerman, H. Problem of reinoculation of human beings with *Spirochaeta pallida*: review of literature. *Am. J. Syph., Gon. & Ven. Dis.* **30**:173-192, 1946.
40. Thomas, E. W., Wexler, G., and Shur, M. Report of chancre developing in patient with cardiovascular syphilis. *Am. J. Syph., Gonor. & Ven. Dis.* **29**:604-607, 1945.
41. Wallman, J. Notes on significance of fever in syphilis with reference to hypopyrexia. *J. Roy. Army M. Corps* **85**:117-122, 1945.
42. Jordon, J. W., and Dolce, F. A. Latent syphilis: study of one hundred and sixty-nine cases observed ten years or more. *Arch. Dermat. & Syph.* **54**:1-18, 1946.
43. Dressler, M. Cardiovascular syphilis: approach to early clinical recognition and early treatment. *Connecticut M. J.* **9**:844-854, 1945.
44. Jackman, J., and Lubert, M. Significance of calcification in ascending aorta as observed roentgenologically. *Am. J. Roentgenol.* **53**:432-438, 1945.
45. Schamberg, I. L. Syphilitic vascular or cardiovascular disease occurring early in adult life following acquired syphilitic infection. *Am. J. Syph., Gonor. & Ven. Dis.* **30**:58-69, 1946.
46. Underwood, L. J. Lumbar puncture headache: statistical analysis of five hundred punctures. *Am. J. Syph., Gonor. & Ven. Dis.* **30**: 264-271, 1946.
47. Heyman, A. Acute syphilitic meningitis: discussion of problems encountered in diagnosis. *Am. J. M. Sc.* **209**:664-671, 1945.
48. Shaffer, L. W. Intensive arsenotherapy of early syphilis. *Arch. Dermat. & Syph.* **52**:147-154, 1945.
49. Trow, E. J., and Dixon, H. A. Intensive treatment of early syphilis with oxophenarsine hydrochloride by multiple injections. *Arch. Dermat. & Syph.* **52**:155-161, 1945.
50. Hoffman, M. M., and Kalz, F. Studies on liver function. I. Liver function in early syphilis before and during massive arsenotherapy. *Am. J. Syph., Gonor. & Ven. Dis.* **29**:596-603, 1945.
51. Thomas, L. J., and Olansky, S. Study of liver function following massive arsenotherapy for syphilis. *Am. J. Syph., Gonor. & Ven. Dis.* **30**:272-278, 1946.
52. Knight, H. C., and Schachat, W. S. Hyperpyrexia in treatment of ocular conditions due to syphilis. *Arch. Ophth.* **35**:271-279, 1946.
53. Bruetsch, W. L. Malaria therapy in syphilitic primary optic atrophy. *J. A. M. A.* **130**:14-18, 1946.
54. Petersen, M. C. Electric shock in treatment of dementia paralytica. *Proc. Staff Meet., Mayo Clin.* **20**:107-112, 1945.
55. Bruetsch, W. L. Public health aspect of malaria therapy of neurosyphilis. *Am. J. Syph., Gonor. & Ven. Dis.* **29**:494-505, 1945.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 33071

PRESENTATION OF CASE

A twenty-seven-year-old engineer entered the hospital because of polydipsia and polyuria.

Six and a half years before entry the patient had had an episode of pain in the right lower quadrant for which an appendectomy was performed. At that time the mesenteric lymph nodes were found to be enlarged. Two months later he was seen by a physician because of anorexia, fatigue, moderate exertional dyspnea and a weight loss from 158 to 146 pounds. He was referred to this hospital for further study.

Examination in the Out Patient Department showed palpable cervical, axillary and inguinal lymph nodes, but none were considered suitable for biopsy. An x-ray film of the chest revealed a sharply outlined lobulated mass, 9.5 cm. at its widest point, occupying the region of the great vessels opposite the pulmonary conus and obscuring the outline of the aorta. The lymph nodes at the lung roots were slightly enlarged. The trachea was not deformed or displaced. The lung fields were clear. On the basis of these findings, the patient was given 600 r of x-ray therapy to the mediastinum and 500 r to the groin and lumbosacral spine. Following this treatment there was marked clinical improvement. Several months later he began to have pain in the low back and left posterior hip, which disappeared after x-ray therapy (600 r). An x-ray film had shown an area of destruction in the sacrum. Several months later, while the patient was in another city, a biopsy of a cervical lymph node was reported as showing Hodgkin's disease. During the following two years enlarged lymph nodes appeared from time to time in the neck, mediastinum, axilla and groin. These were treated as they appeared by radiation, with rapid subsidence.

Four years before entry the patient complained of generalized itching, particularly on the legs. At that time there were lymph nodes, 1 or 2 cm. in diameter, in the neck and inguinal regions. The spleen extended to the costal margin on inspiration. X-ray examination of the chest was negative; there were no enlarged mediastinal shadows. He was given generalized as well as local radiation, and received 1.5 cc. of radioactive phosphorus (equivalent to 0.44 mc.) intravenously. The itching of the skin was benefited by a constant intake of 50 cc. of viosterol (500,000 units of vitamin D) a week. This dosage of viosterol was continued until entry. Two months later the patient complained of pain in the low mid-back and down the thighs. X-ray examination of the lower spine showed areas of increased density in the tenth and twelfth dorsal and the first, second and third lumbar vertebras. There was also a small soft-tissue mass in the paravertebral space on the left of the tenth dorsal vertebra, and some involvement of the medial portion of the right ilium. Radiation gave symptomatic relief, but the x-ray findings remained unchanged. Three years before entry the appearance of scattered warts on the legs was noticed. Six months later the only complaint was precordial pain occurring after severe exertion. There were fine inspiratory rales at the left apex posteriorly, and a chest film revealed a small, semicircular, soft-tissue mass between the left eighth and ninth ribs near the vertebra. Otherwise, the lungs were clear. After local radiation the symptoms disappeared, and the patient felt well, the weight reaching 174 pounds. A year before admission he had an attack of herpes zoster over the right side of the neck, upper chest and upper shoulder.

Four weeks before entry, the patient began to feel weak, tired and feverish. He lost his appetite and developed an annoying dryness of the mouth and an increasing thirst. He drank about 4 liters of water a day and passed large amounts of light-colored urine, voiding five or six times during the night. Occasionally, he felt an urge to urinate even though the bladder was not distended. He also became constipated, having only one bowel movement in three to five days, despite the taking of cascara and mineral oil. The eyes became sensitive to light and burned, particularly when he was doing close work. On waking in the morning he had some retching, but there had been no actual vomiting. For several days before entry the patient was forced to go to bed because of increasing malaise, weakness and drowsiness. He had vague muscle aches in the legs and diffuse headaches occurring about once a day, increased by motion of the head. The day before entry he had stiffness and aching in the lumbosacral region. While driving to the hospital, the patient found himself "weaving" all over the street and was unable to judge distances, so that several times he collided with the car ahead of him.

Physical examination showed a well nourished patient who appeared both acutely and chronically ill. He was drowsy and dozed off quietly after the examination. The respirations were deeper than normal. There were bilateral, soft, nontender cervical lymph nodes measuring about 1.5 cm. in diameter. The axillary and epitrochlear nodes were not

palpable. In the left groin there was a 5-cm., soft, elongated, nontender mass. The heart and lungs were normal. The liver edge was percussed 2 to 3 cm. below the costal margin. There was a hydrocele 9 cm. in diameter on the left side. The extremities were normal except for scattered large warts over the legs. Examination of the cranial nerves was negative. The pupils were normal and reacted well to light and accommodation. The neck was stiff, and the Kernig test was positive bilaterally. The finger-to-nose test was negative. There was no adiadokokinesis, and no muscle weakness. The tendon reflexes were normal. The abdominal reflexes were absent. The plantar response was flexor bilaterally; sensation was normal.

The temperature was 101°F., the pulse 104, and the respirations 24. The blood pressure was 130 systolic, 85 diastolic.

Examination of the blood disclosed a red-cell count of 2,940,000, with a hemoglobin of 10.5 gm., and a white-cell count of 4500, with 86 per cent neutrophils. The total protein was 5.6 gm. per 100 cc., with an albumin-globulin ratio of 1.5. The nonprotein nitrogen was 52 mg., the calcium 12.6 mg., the phosphorus 4.3 mg., the alkaline phosphatase 1.9 mg. and the fasting blood sugar 145 mg. per 100 cc., and the carbon dioxide 30.5 milliequiv. per liter. The prothrombin time was 22 seconds (normal, 14 seconds). The van den Bergh reaction and a cephalin-flocculation test were negative.

The urine was slightly cloudy and straw colored. The specific gravity was 1.005. The sediment contained 8 to 12 white cells and a few granular casts per high-power field. No sugar or albumin was found. A urine culture yielded abundant colonies of *Staphylococcus albus* and alpha-hemolytic streptococcus. The phenolsulfonephthalein test showed 45 per cent excretion in two hours. The urinary calcium excretion was 1290 mg. in twenty-four hours. A stool was brown, liquid and guaiac negative.

A lumbar puncture revealed an initial pressure equivalent to 150 mm. of water, with normal dynamics. The fluid was clear and colorless and did not clot on standing. There were 450 cells per cubic millimeter, of which 80 to 90 per cent were lymphocytes and the remainder polymorphonuclears. The total protein was 58 mg., the sugar 70 mg. and the chloride 111 mg. per 100 cc. The gold-sol curve was 0001122100. Smears of the spinal-fluid and urinary sediment were negative for acid-fast organisms.

During a twenty-four-hour period following the intramuscular ingestion of 1 cc. of pitressin tannate, the fluid intake fell from 4500 cc. to 2750 cc., and the urinary output went from 3500 to 2000 cc.

An x-ray film of the chest showed a miliary nodular process throughout both lungs. There was also an area of calcification in the anterior aspect of the right side of the chest close to the sternum. A skull film showed multiple areas of calcification in the left frontal region.

On the seventh hospital day the patient became disoriented and increasingly drowsy. He developed a coarse tremor of the fingers on extension. A second lumbar puncture revealed an initial pressure equivalent to 240 mm. of water. The fluid had a ground-glass appearance and formed a pellicle on standing. A smear showed one definite acid-fast organism; a subsequent smear on another specimen was negative. The spinal-fluid culture was negative. Slit-lamp examination showed a keratitis similar to that seen in hypercalcemia.

During the fourth week in the hospital the patient began to lose ground rapidly. He had nausea, vomiting and persistent hiccough. On the thirty-third hospital day he became comatose. He developed a right facial palsy, and the left pupil became dilated. The temperature rose to 104.5°F., and the respiratory rate to 45. The patient died on the thirty-fourth hospital day.

Differential Diagnosis

Dr. Richard J. Clark: This patient's illness may be considered to have started with the right-lower-quadrant pain for which an appendectomy was performed and following which definite signs of debility appeared. We are told in the early portion of the protocol that a biopsy showed Hodgkin's disease. Certainly, all the preliminary evidence of lymph-node enlargement, including para-aortic and mesenteric nodes, evidence of bone involvement, response to radiation and appearance of pruritus are consistent with this reported diagnosis. I shall accept this as a basic working diagnosis in spite of the danger of so doing in these exercises.

We note that the patient was placed on a large dose of vitamin D, — 500,000 units a week, — which he continued over a period of four years. This is a matter to be kept in mind for future consideration. Precordial pain is mentioned only once, and there were no other findings referable to the heart; therefore, I shall dismiss this as evidence of recurring chest tumor. The development of herpes zoster is a frequent occurrence in Hodgkin's disease.

Four weeks prior to entry we are first told of feverishness, which is perhaps surprising. In long-standing Hodgkin's disease the presence of fever would have been expected earlier. This raises the possibility of some complicating infection. Evidence of polyuria then appeared, and I shall discuss this in further detail subsequently. The urgency of urination and increasing constipation raise the possibility of a pelvic mass. Shortly before entry evidence of central-nervous-system involvement — consisting of headache, photophobia, stiffness of the back and unsteadiness — first appeared, and on arrival at the hospital we find objective confirmation in the patient's drowsy and dazed condition.

Neurologic examination revealed evidence of meningeal involvement without positive evidence of any lesion in the brain proper.

Laboratory studies indicated a blood picture compatible with chronic Hodgkin's disease. There was some elevation of the nonprotein nitrogen, an elevated calcium and a normal phosphorus with a low phosphatase. The blood sugar was elevated on the one determination given, and yet we are not told of any glycosuria; this raises the bare possibility of involvement of the pancreas by Hodgkin's disease. The urinary calcium increase, as I understand it, was tremendous. The normal value is 150 to 200 mg. in twenty-four hours. There was evidently urinary-tract infection and possibly a decreased renal function, although we could tell more about that if we knew what the fractional phenolsulfonephthalein excretion showed. There was a low urinary specific gravity, but with the polyuria this is not surprising. We may judge from the total picture that there was probably some decrease in the renal function. The spinal fluid showed an increase to 450 cells per cubic millimeter, chiefly lymphocytes, an increase in protein, a normal sugar and only a slightly lowered chloride. These findings certainly give evidence of some type of meningeal involvement. The sugar content was too normal for a bacterial infection. Could this have been a tuberculous meningitis? We know that active tuberculosis does occur in association with Hodgkin's disease. On the other hand, the spinal-fluid findings are against tuberculosis in that the sugar was rather higher than one would expect to see in this condition, and the chloride was not so low as one would anticipate. For these reasons, it is my inclination to say that Hodgkin's involvement of the meninges is likely. We know that this does occur, and I am told that this spinal-fluid picture is compatible with a lymphomatous involvement of the meninges.

The x-ray report of a nodular process throughout the lung is slightly disquieting. Again, the possibility of tuberculosis looms, but lymphoma may produce a diffuse nodular involvement and we have seen cases in which quite definite evidence of previous pulmonary lymphoma cleared under x-ray therapy and I tend to hold to this latter interpretation. In such cases there is evidence of diffuse calcium deposition in various areas of the body. Calcification may occur in scarred areas of treated lymphoma, and this finding is not a strong point for tuberculosis in the case under discussion.

We are given evidence of increasing cerebrospinal pressure and meningeal involvement, with possible involvement of the brain proper. A repeated spinal-fluid examination showed a pellicle on standing; this is always suggestive of tuberculosis, but may occur in any fluid with a high protein content. Finally, our dilemma is climaxed by the report of a single acid-fast organism. If this is true it is positive evidence of concomitant meningeal tuberculosis.

Dr. Lewis K. Dahl: One of the students detected the organism in the smear, and its presence was confirmed by several of the house officers.

Dr. Clark: One cannot laugh off a definite acid-fast organism, if it was found. May we see the x-ray films?

Dr. Richard Schatzki: The majority of the old films are not here. One film taken about three years ago shows for all practical purposes a normal chest. This chest film, taken when the patient entered the hospital, shows fine miliary nodules of approximately equal size scattered throughout both lung fields and rather homogeneously distributed. We have another film taken a month later, which shows that the lesions had not grown since that time. As a matter of fact they look somewhat smaller, but since the patient was then extremely ill, the films could not be taken in the same fashion. Certainly the lesions have not become larger. The skull shows flecks of calcium, which stereoscopically were thought to be in the inner table or in the dura.

Dr. Clark: Does the skull show evidence of general decalcification?

Dr. Schatzki: It does not.

Dr. Clark: None of the other bones that are seen show any definite evidence of decalcification?

Dr. Schatzki: No.

Dr. Clark: I have committed myself to a primary diagnosis of Hodgkin's disease, to which I shall stick and which I believe will be found diffusely. I shall not take the time to discuss other differential diagnoses in detail. We might for a moment think of the possibility of Boeck's sarcoid. It mimics Hodgkin's disease and involves all the tissues in question, but the lack of any hyperglobulinemia and the general course of the disease make that diagnosis unlikely.

Beyond the basic diagnosis comes the question of several complicating factors. In the first place there was a high blood calcium, and the question arises whether this patient had a concomitant hyperparathyroidism. The chemical findings are rather against it. The elevated blood calcium and the high urinary calcium are consistent, but the presence of a relatively high phosphorus and a low phosphatase militate against this diagnosis, as does the absence of decalcification in the bone. Recently, an increasing number of cases of vitamin D poisoning have been reported, particularly in people taking large doses of vitamin D for arthritis. Symptoms have been described similar to those experienced by this patient — namely, drowsiness, polydipsia, polyuria, dizziness and anorexia in conjunction with high blood and urinary calcium and renal insufficiency. I believe that this patient had some degree of vitamin D intoxication, with renal insufficiency, which may have contributed to the extremely high

urinary calcium output. The destruction of bone in any metastatic neoplasm such as lymphoma, however, could in itself produce a high blood calcium and a high urinary calcium. I believe that a combination of these two factors was at play in this particular case. We might, however, have expected more evidence of decalcification of the bones from vitamin D over this long period than is demonstrated.

Did the patient have diabetes insipidus? The polyuria and the polydipsia were not so extreme as those seen in some cases in which the intake ranges from 8 to 10 liters a day. However, an intake of 4 or 5 liters may be consistent with this diagnosis. The hypercalcemia in itself may have been a cause of the polydipsia and polyuria. On the other hand, the response to pitressin suggests a true diabetes insipidus. Hodgkin's disease has been known to involve the hypophysis and to produce this condition. We also know that basal meningitis in itself may cause symptoms similar to those of diabetes insipidus. We have strong evidence that some process was involving the cranium, and I assume that lymphoma was found in the meninges and in the substance of the brain. I think that this process had involved either the hypothalamic region or the hypophysis. It seems likely that, in the terminal stages, the process broke through from the hypothalamic region into the meninges, and that event may have been the start of the meningeal process.

The question whether there was also a tuberculous process, miliary in nature, with lung involvement, remains open. It is a definite possibility, and if there was a positive acid-fast organism, we must assume that tuberculosis was present. Even though tuberculous meningitis may have been present, I shall hold to a lymphomatous involvement in the central nervous system in addition. The kidneys may well have shown some damage — either lymphomatous or on the basis of calcium deposition with secondary infection. The finding of renal calculi would not be surprising. Various areas of metastatic calcification were doubtless found.

Dr. Donald S. King: The interesting thing about the x-ray studies is the marked improvement demonstrated in the film. The patient was much better after a month than at the beginning. Dr. Schatzki, have we ever seen that appearance with Hodgkin's disease?

Dr. Schatzki: No; we have had patients with disseminated involvement of the lung by Hodgkin's disease, but usually the lesions were larger and not so homogeneous as these.

Dr. King: This case was more consistent with miliary tuberculosis than with Hodgkin's disease?

Dr. Schatzki: Yes.

Dr. King: It is interesting to see this change because if the patient had had streptomycin as was suggested we should have ascribed the improvement to the streptomycin.

Dr. Allan M. Butler: Unless this patient was bedridden, which he may well have been for a while, and suffering atrophy of disuse, which the x-ray films do not indicate, the amount of vitamin D given probably would not have caused any trouble. If such a quantity of vitamin D is administered today it should not be given as viosterol but as one of the concentrated preparations.

Dr. David G. Cogan: I was interested in this patient because of the eye changes. They are readily overlooked unless one searches for them specifically. A slit lamp is not necessary to see the changes. They consist of a deposition of white opacities of the cornea in the palpebral fissure adjacent to the limbus, and in histologic sections they stain like calcium. This patient represents one of seven whom I have seen at the request of Dr. Albright; all had a high blood calcium, but none of them had hyperparathyroidism unless uremia was also present. Three of these patients had a high blood calcium associated with sarcoid, and the other four had a high blood calcium associated with hyperparathyroidism as well as uremia. It is an interesting finding in patients with hypercalcemia that is not generally recognized.

Clinical Diagnoses

Miliary tuberculosis.
Tuberculous meningitis.
Hodgkin's disease.
Vitamin D intoxication.

Dr. Clark's Diagnoses

Hodgkin's disease, with diffuse involvement, including hypophysis and meninges.
Superimposed tuberculous meningitis?
Metastatic calcification.
Vitamin D intoxication.
Diabetes insipidus.

Anatomical Diagnoses

Tuberculous meningitis.
Miliary tuberculosis of lungs.
Tuberculosis of left adrenal gland and thoracic duct.
Vitamin D intoxication.
Metastatic calcification of kidneys and (?) posterior lobe of pituitary body.
(*Diabetes insipidus.*)
Malignant lymphoma, Hodgkin's type, of retroperitoneal lymph nodes.

Pathological Discussion

Dr. Tracy B. Mallory: Autopsy on this patient showed both Hodgkin's disease and tuberculosis, the tuberculosis being much the more prominent of the two. In fact the only grossly obvious Hodgkin's focus that we found was in the retroperitoneal lymph nodes, which were considerably enlarged. The lungs were peppered with miliary tubercles, all

of which were firm and fibrous, with a minimal amount of caseation. It is quite possible that in the initial acute stage they were considerably larger than at the time of autopsy and that they actually shrank, as the x-ray films suggest. Examination of the brain showed an extensive tuberculous meningitis, which Dr. Kubik will discuss in a moment. In any case of miliary tuberculosis one is always interested in the source. Miliary tuberculosis is not a primary disease but is secondary to some older focus of the disease. A careful search throughout the body seemed to show only one possible source, the left adrenal gland, where a caseous tubercle has frequently been described following excessive dosage of vitamin D.

DR. CLARK: Was there anything in the pancreas?

DR. MALLORY: No.

DR. CHARLES S. KUBIK: In this case there was extensive exudate chiefly over the base of the brain, with numerous small tubercles, which were easily seen with the naked eye and from which the diagnosis of tuberculous meningitis could be made conclusively at autopsy. The more usual finding is only a small amount of basilar exudate, with little exudate anywhere else, and a number of characteristic tubercles. In practically every case there are

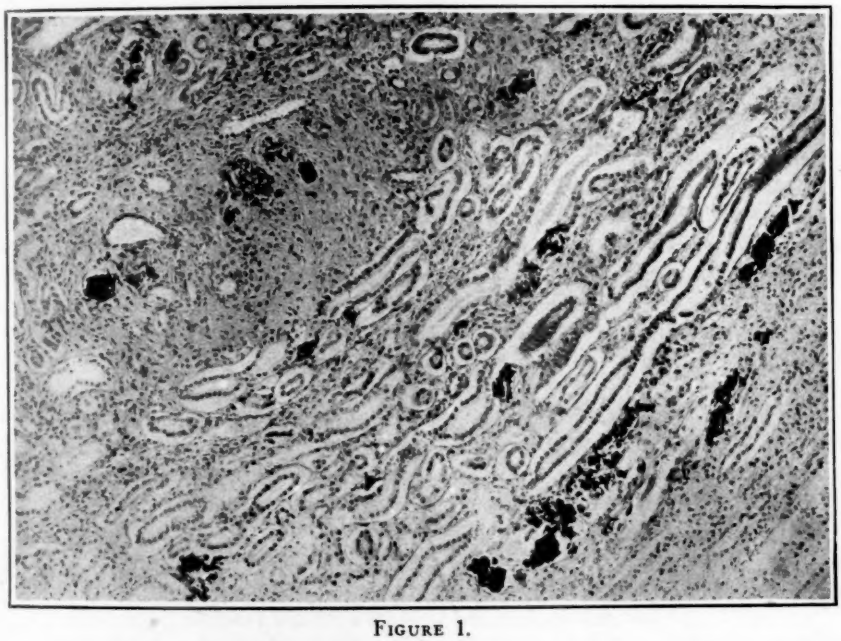

FIGURE 1.

somewhat over 1 cm. in diameter was found that was invading a lymphatic vessel in the periadrenal fat. The rest of the tuberculosis seemed to be fresh and acute. The surprise of the autopsy was that the thoracic duct was completely occluded, almost from top to bottom, with caseous material.

The posterior lobe of the pituitary body showed a small lesion, a spicule of dense calcium, one part of which had been slightly organized into bone. This was surrounded by a mass of necrotic polymorphonuclear cells. There was nothing about it to permit a positive diagnosis of tuberculosis. Since calcification was found in other areas there is a possibility that this was a focus of metastatic calcification and not a tuberculous lesion. The kidneys were large, and on gross section innumerable small white specks could be seen, mostly in the pyramids. Sections showed microscopically that these were masses of calcareous material lying close to but always just outside the collecting tubules and occasionally the distal convoluted tubules (Fig. 1). The appearance is characteristic of the type of renal calcification that tubercles of the ependyma of the lateral and third ventricles, particularly the latter. The ventricles are enlarged. On microscopical examination there is likely to be infiltration of the cranial and spinal nerves and, in some cases, of the optic chiasm or tracts. In the case under discussion there was degeneration in one of the third cranial nerves, which probably accounted for the large pupil noted during life. The infection often extends through the arachnoid to the inner surface of the dura and through the pia into the underlying tissues.

CASE 33072

PRESENTATION OF CASE

A forty-eight-year-old married woman entered the hospital because of unexplained fever.

The patient had been well and active until six months before entry, when she began to complain of fatigue. Three months later she developed dyspnea and noticed that she was losing weight. Six

weeks before entry a physician discovered that she had anemia; the white-cell count was 25,000, with an increase in polymorphonuclear leukocytes. The temperature was normal at that time. Two weeks later she developed night sweats and a temperature swinging up to 105°F. She was admitted to a hospital, where the liver edge was thought to be palpable one fingerbreadth below the costal margin; it was not tender. The red-cell count was 2,800,000, with a hemoglobin of 47 per cent, and the white-cell count 20,000 to 40,000. The sedimentation rate was elevated. A blood culture yielded Alcaligenes (type undetermined). The urine showed a + test for albumin, and the sediment contained occasional white cells. There was no urobilinogen. The icteric index was normal. A cephalin-flocculation test gave a + reaction, and the alkaline phosphatase was 5.2 Bodansky units. Agglutination tests for typhoid, brucellar and heterophil antibodies were negative. X-ray films of the chest and of the gastrointestinal tract and a pyelogram were normal, as was an electrocardiogram. Examinations of the stools for amebas were negative. For four weeks before entry the liver increased progressively in size, with occasional bouts of soreness, and the temperature ranged from subnormal to 105°F. During the periods of high temperature the patient was frequently disoriented. With a fluid intake of 2400 to 4000 cc., the urinary output ranged from 300 to 900 cc. Neither 11 gm. of sulfadiazine over a forty-eight-hour period nor 3,480,000 units of penicillin administered in two courses of eight days each had any effect on the temperature. An eleven-day course of sodium salicylate, with a total daily dosage of 7 to 60 gm., held the temperature below 102.4°F. This therapy was terminated because of a drop in urinary output. No further reduction in the temperature was obtained with 40 mg. of intramuscular emetine hydrochloride given intramuscularly, and the patient grew progressively worse. A week before entry she had slightly icteric scleras and bile in the urine for a day. She also developed slight edema of the ankles and sacrum. Since the onset of the illness, she had lost about 10 pounds in weight.

On admission to this hospital the patient was moderately disoriented, drowsy, dyspneic and dehydrated. The scleras were slightly icteric. There was no palpable lymphadenopathy. The right leaf of the diaphragm was elevated to the inferior angle of the scapula. There were dullness, diminished breath sounds and a few crackling rales over the lower half of the right chest. The heart sounds were rapid and forceful. A Grade II systolic murmur was heard over the precordium. The abdomen was tense and distended. The liver edge was palpable 4 to 5 cm. below the costal margin and was extremely tender. The spleen could not be felt. There was no fluid wave or shifting dullness. There was moderate edema over the ankles.

The temperature was 101.5°F., the pulse 110, and the respirations 27. The blood pressure was 114 systolic, 68 diastolic.

Examination of the blood showed a hemoglobin of 10.6 gm. and a white-cell count of 20,600, with 87 per cent neutrophils. The nonprotein nitrogen was 18 mg., and the serum protein 5.7 gm. per 100 cc., with an albumin globulin ratio of 1.17; the chloride was 92 milliequiv. per liter. The prothrombin time was 39 seconds (normal, 19 to 21 seconds); the serum van den Bergh and the blood Hinton reaction were negative, as were four blood cultures. The urine was normal except for a + test for albumin.

X-ray examination revealed a high diaphragm on the right, obscured by increased density in the lower lung field. There was also evidence of fluid extending upward along the lateral chest wall. Beneath the right half of the diaphragm there was a ground-glass density extending down to the right lower quadrant of the abdomen. The right lobe of the liver appeared to reach almost to the iliac crest. The soft-tissue outlines of the entire abdomen were partly obliterated by increased density. No gas was seen in or about the area of the liver. There was no evidence of dilated loops of bowel.

On the third hospital day the right side of the chest was aspirated high in the axilla, and 50 cc. of bloody fluid containing 670,000 red cells and 12,800 white cells per cubic millimeter was obtained; 80 per cent of the white cells were polymorphonuclears. Aspirations under the twelfth rib posteriorly and under the costal margin anteriorly were negative.

On the fifth hospital day an operation was performed.

Differential Diagnosis

Dr. Chester M. Jones: It is obvious that since this patient was operated on she was thought to have a surgical condition that was remediable. I do not believe that she was operated on solely for diagnosis. The history that she presented was one of gradual weakness and a spiking temperature that slowly increased in severity, but she had no chills at any time. The liver enlarged rather rapidly and was tender, but there was no associated jaundice. During the course of the disease, fluid developed in various parts of the body, with edema of the extremities, hydrothorax and probably ascites. There was a considerable leukocytosis, the white-cell count varying from 20,000 to 40,000 cells, always with 80 per cent neutrophils. There were no comments regarding either the presence of toxic granules or any abnormality in the type of white cells seen.

With a spiking temperature such as that noted in this case, the question must always be raised concerning the underlying mechanism. If infection, what type of infectious process could it have been? If not infection, what other process could have given such a persistent elevation of temperature? It is

important then to point out some apparent facts. Jaundice was absent, and for this reason the clinical picture was not that of obvious intrahepatic infection, such as an infectious hepatitis. One can be sure that the infectious process did not develop so rapidly that jaundice did not have time to appear. The duration of the fever and of the hepatic enlargement was several months. It is more reasonable to assume that an infectious process would have been associated with focal areas of infection in the form of multiple liver abscesses or possibly a single large abscess. It is possible that such a spotty type of infection also involved the vascular bed of the liver, with resulting thrombophlebitis. I am sure that infectious hepatitis was not present. Other acute infections, such as brucellosis, do not seem likely, since the clinical course was quite atypical for brucellosis and agglutination reactions were negative. Infectious mononucleosis could present such a picture, but the blood studies are distinctly against such a diagnosis.

What other possibilities are there? One is a new growth, such as a lymphoma of some sort, Hodgkin's disease of the reticulum-cell type or even leukemia. Any one of these may be associated with hepatic enlargement and with a fever that simulates sepsis. Against such a diagnosis was the absence of adenopathy and splenic enlargement and the blood findings. Could the hepatic enlargement and fever have been due to metastatic neoplasm, carcinomatous or otherwise? There is no evidence of a malignant lesion elsewhere. X-ray studies of the gastrointestinal tract were negative, and there were no abnormalities in the urine. There is no clue regarding the possibility of cancer, so far as I can see, with the possible exception of the bloody chest tap.

Could the patient have had cirrhosis of the liver? In such cases fever, pain and an enlarged liver are observed, but the clinical picture presented in the case under discussion was not, to my mind, at all suggestive of this type of hepatic disease. Even in the presence of a superimposed hepatoma, it seems to me that the febrile course was most unusual and probably against such a diagnosis.

If liver abscess is considered, one must mention the possibility of a solitary abscess, conceivably due to amebic infection. Against such a diagnosis was the lack of response to an adequate dose of emetine. In most cases the therapeutic response to this drug is dramatic, and I therefore believe that such a possibility can be ruled out. Furthermore, no cysts or parasites were found in the stools. If multiple liver abscesses caused the septic fever, their possible source must be sought. In most cases the abscesses are secondary to an infectious process related to appendicitis or infection of the biliary tract. We occasionally see hepatic abscesses associated with ulcerative colitis, but this, of course, was obviously not present in the case under discussion.

There could have been a septicemia with metastatic liver abscesses, but four blood cultures were negative. In my experience, it is unusual to have multiple liver abscesses associated with fever of this type without the frequent recurrence of chills. It seems to me that such a possibility should be considered with, let us say, a thrombophlebitis of the portal radicles or even of the intrahepatic veins or of the hepatic vein itself. If such an infection was present, one must again inquire its source. In most cases the process is associated with thrombophlebitis elsewhere, or with focal infection or malignant involvement of the biliary tract with compression of the venous channels in the liver, either hepatic or portal.

The chest findings indicate only a high diaphragm on the right with fluid in the right pleural cavity and with a tremendous enlargement of the liver. I shall not waste time in discussing the x-ray films, unless there is a suggestion of some other findings.

Dr. James R. Lingley: That is all they show.

Dr. Jones: The description of the abdominal films is quite typical of ascites — that is, a ground-glass appearance with more or less obliteration of the soft-tissue outlines. Am I correct?

Dr. Lingley: Yes.

Dr. Jones: There were ascites and a right hydrothorax. A chest tap showed 670,000 red cells and 18,000 white cells per cubic millimeter, with 80 per cent polymorphonuclear leukocytes. The presence of blood in the pleural fluid may have been due to trauma to a vein but definitely suggests the possibility of cancer or tuberculosis. I have never seen a clinical picture such as this due to tuberculosis. The fluid in the pleural cavity, I believe, could have been associated with a thrombus of a venous radicle in the region of the diaphragm. Most of the trouble was certainly under the diaphragm, and a subphrenic abscess was properly suspected. The patient was tapped in the twelfth interspace and also anteriorly to determine if pus could be located under the diaphragm. So far as the x-ray study is concerned, there could have been a subphrenic abscess with irritation in the pleural cavity above, but such a process does not explain the obvious hepatic enlargement. It is evident that I am groping for an explanation of a mysterious clinical picture.

I have one or two other comments. There is not too much information in the record about liver function, but the fact that the prothrombin time was prolonged suggests that the liver was seriously damaged. There are other factors, such as diarrhea, to explain the prolongation of the prothrombin time. The serum albumin and protein were low. These figures could go with interference with hepatic function and help in part to explain the accumulation of fluid in various parts of the body. They do not have diagnostic significance, however. If straightforward infection had been present in or around the

liver, one would expect marked toxic granulation in the white cells. No such observation was made. I believe that it is possible, therefore, to veer away from focal infection in the liver but not from infection adjacent to the liver. I have already suggested the possibility of thrombophlebitis, and I think that there were areas of thrombophlebitis in the portal circuit, in the body of the liver itself or in the hepatic veins at the entrance of the vena cava. I have a suspicion that something like Chiari's syndrome may have been present. This curious clinical picture is always secondary to another process — sometimes an infection and sometimes a metastatic neoplasm infiltrating the liver and compressing the venous channels. I am inclined to doubt a really diffuse infiltrating cancer in the liver because of the complete absence of jaundice. I am more inclined to think that there may have been a malignant process outside the liver. At a guess, I suggest that it might have been a lymphomatous type of neoplasm. I do not believe that there was a single hepatic abscess or multiple hepatic abscesses or that operation was performed with the expectation of finding focal sepsis in the liver. The failure to obtain a therapeutic response from penicillin in no way rules out intrahepatic infection, because undrained sepsis in the liver will not respond satisfactorily to antibiotics.

So far as I am concerned, the absence of chills makes me believe that a primary infectious process in the liver was not present. Pylephlebitis, of course, is a possibility, but I cannot imagine what the initial cause was.

Finally, therefore, I lean to the possibility of some neoplastic disease around the liver, causing its rapid enlargement and fever but little serious interference with liver function. I shall leave it there, but merely add that I believe that what was found at operation was not amenable to surgery.

Dr. Wade Volwiler: I was asked to see this patient to consider the possibility of doing a blunt-needle biopsy of the liver to make a histologic diagnosis. The patient was extremely ill, disoriented and delirious and looked as if she would die at any moment. It seemed, in spite of the absence of chills, that focal infection within the liver was entirely possible and that therefore one would not want to do any procedure that might spread sepsis. Also, the prothrombin time was prolonged, and such a procedure would not be safe without a transfusion. We went for the argument in favor of infection — hook, line and sinker.

Dr. Beverly T. Towery: Is not the absence of jaundice against Chiari's syndrome?

Dr. Jones: No; Kelsey and Comfort* have reported 20 cases in only a small number of which jaundice was present. The syndrome can occur perfectly well without jaundice.

Clinical Diagnosis

Liver abscess?
Subphrenic abscess?

Dr. Jones's Diagnosis

Neoplastic disease around liver, with intrahepatic thrombophlebitis.

Anatomical Diagnosis

Metastatic epidermoid carcinoma of liver, primary source undetermined.

Pathological Discussion

Dr. Tracy B. Mallory: I do not know whether the Pathology Department is able to explain this case completely. We can, however, state the major diagnosis. The patient was operated on, as Dr. Jones suspected, in the hope that a subdiaphragmatic or liver abscess would be found. For that reason the exploration was done posteriorly; the surgeon came down on the superior surface of the liver, which was studded with tumor masses of metastatic carcinoma. A biopsy was performed. The tumor was highly undifferentiated, but I believe that it was an epidermoid carcinoma. This histologic structure was quite consistent with a bronchiogenic carcinoma, but the patient left the hospital without our ascertaining the primary focus.

Dr. Jones: Do you agree that there might have been enough infiltration into the hepatic substance or around it to produce a partial venous block, thus causing many of the symptoms noted?

Dr. Mallory: That is possible but unusual in metastatic carcinoma. In primary liver-cell carcinoma, venous invasion is frequent, and there is no reason why it could not occur with metastatic disease.

Dr. Jones: If I remember correctly this is just what happened in several cases of metastatic cancer reported by Kelsey and Comfort.

*Kelsey, M. P., and Comfort, M. W. Occlusion of hepatic veins: review of twenty cases. *Arch. Int. Med.* **75**:175-183, 1945.

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THE ALCOHOLIC PATIENT

Ever since man first observed the phenomenon of fermentation and noted the effect of its products on the human body, he has been faced with the problem of alcoholism. Only in recent years, however, and still far from fully, has the victim of alcohol, like the sufferer from mental disease, been considered as an ill person.

The consumption of strong drink is again on the increase, and with it we are undergoing a resurgence — we hope a more intelligent one than ever before — in our concern for the drunkard. Contributing to knowledge of the subject is the report issued in 1945 by the special commission appointed by the Legislature to investigate the problem of alcoholism in Massachusetts.

There are now, it is estimated, some 20,000 alcohol addicts in the Commonwealth, and alcohol is largely responsible, in one way or another, for the commitment of 25 per cent of the population of our mental hospitals; in addition, alcoholism is responsible for 26 per cent of the cases handled by the Boston Council of Social Agencies. Alexander, Moore and Leary* found on an analysis of all deaths due to toxic substances from 1928 to 1937 that ethyl alcohol was the cause in 52 per cent.

Eighty out of every hundred prisoners in the Charles Street Jail, according to a recent report, are under arrest for drunkenness, and His Honor, Mayor James M. Curley, has made the sagacious suggestion that the jail be converted into a hospital for alcoholic patients, the cost of its maintenance to be met by increasing the license fee for the sale of alcoholic beverages by $500 annually.

The proposition that those who profit by the sale of liquor be made at least partly responsible for the cost of its by-effects seems fair. It recognizes also the thesis that alcoholism is a medical rather than a penologic problem. As evidence that an enlightened view of alcoholism is not universal comes a statement from the Massachusetts Commissioner of Probation and others urging repeal of the statute allowing persons arrested for drunkenness to be released without punishment for the first four offenses. With alcoholism considered as a disease, the word "punishment" is objectionable.

The Charles Street Jail, obviously, is scarcely a suitable building for a hospital, nor is it yet clearly demonstrated that more in-patient facilities are required for alcohol addicts. If such a need can be demonstrated, the recently proposed program calling for the utilization of the Bridgewater State Farm is more to the point and deserves careful scrutiny. There is no question that more clinic facilities of one sort or another are necessary.

What is definitely in order is a recognition of the facts, by the medical profession, as well as by others, that alcoholism is a disease, that, as with other diseases, its prevention is more effective than its cure and that the place of the physician is with the various agencies that are striving toward that end.

*Alexander, L., Moore, M., and Leary, T. Deaths from poisoning: incidence in Massachusetts. *J. Crim. Psychopathology* 3:100-111, 1941.

RETIREMENT PROGRAM FOR HOSPITAL EMPLOYEES

IN THESE days when nonprofit hospitals throughout the country are faced with varied difficulties in obtaining suitable employees, any constructive plan that has for its object the improvement of working conditions for these workers deserves serious consideration. Recently, Mr. John H. Hayes, president-elect of the American Hospital Association and chairman of its Pension Committee, has announced a retirement program for employees in nonprofit hospitals. He points out that hospital workers are not now covered by benefits of the Social Security Act and that this is one reason why hospitals are at a disadvantage in maintaining a high grade of personnel. In the preliminary studies of the American Hospital Association, it was found necessary to establish a plan that could be easily fitted in with Social Security payments when and if the federal laws were changed to include workers in hospitals. It was also kept in mind that the contributions should be on a modest basis to fill the needs of both small and large hospitals and that provision should be made for transferring benefits from one hospital to another.

The final plan was developed in co-operation with the National Health and Welfare Retirement Association. It provides for joint employee and employer contributions, the optional provision by the hospital of benefits for past service, fully vested rights for retirement purposes to the employer's contributions and transferability between hospitals that are members of the plan. In case of death the employee's contributions plus interest are paid to his beneficiary. All permanent employees over twenty-five years of age, with one year or more of service, are eligible to join provided that the hospital votes to make the payments on a payroll-deduction basis.

The National Health and Welfare Retirement Association is a nonprofit corporation organized by community chests and various national welfare organizations and licensed under the insurance laws of the State of New York. Mr. Gerard Swope is chairman of the Board of Trustees, which is composed of sixty representatives from all parts of the country, including all the members of the Pension Committee of the American Hospital Association. The association started operations on October 1, 1945, and employer-employee contributions are already being received at the annual rate of $2,000,000.

It is believed that this scheme may well be a helpful step in re-establishing better relations among hospital employees and employers. It should also be of assistance in attracting a better class of workers to fill these much needed positions.

MASSACHUSETTS MEDICAL SOCIETY

BUREAU OF CLINICAL INFORMATION

All secretaries of various medical groups, such as special societies and alumni associations, are requested to notify the Bureau of Clinical Information regarding scheduled meetings, annual dinners and so forth. If such data are on file, it is hoped that duplication of dates can be avoided.

DEATHS

HARE — Charles H. Hare, M.D., of Boston, died January 21. He was in his eighty-fifth year.

Dr. Hare received his degree from Harvard Medical School in 1889. He became interested in gynecology and limited his practice to that specialty, having retired more than a decade ago. He was a member of the Boston Obstetrical Society and a fellow of the American College of Surgeons and the American Medical Association. During his period of active practice he had been a member of the staffs of the Free Hospital for Women, Massachusetts Women's Hospital, St. Elizabeth's Hospital, Boston Dispensary, Carney Hospital and Quincy City Hospital.

PHILLIPS — Wilson F. Phillips, M.D., of Dorchester, died January 29. He was in his seventy-fifth year.

Dr. Phillips received his degree from Boston University School of Medicine in 1898. He was a fellow of the American Medical Association.

His widow survives.

SHEFFERD — Jeannette M. Shefferd, M.D., of Fall River, died October 25.

Dr. Shefferd received her degree from Creighton University School of Medicine, Omaha, Nebraska, in 1912. She was a member of the New England Otological and Laryngological Society and a fellow of the American Medical Association.

TILDEN — Irving N. Tilden, M.D., of Mattapoisett, died November 3, 1946. He was in his seventy-sixth year.

Dr. Tilden received his degree from Harvard Medical School in 1899. He was a former councilor of the Massachusetts Medical Society and was a fellow of the American Medical Association.

His widow and a son, Dr. Benjamin R. Tilden, of Marion survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR DECEMBER, 1946

Résumé

Diseases	December 1946	December 1945	Seven-Year Median
Chancroid	0	2	*
Chicken pox	1331	900	1511
Diphtheria	88	21	20
Dog bite	556	409	517
Dysentery, bacillary	4	12	12
German measles	68	61	68
Gonorrhea	316	467	335
Granuloma inguinale	0	0	*
Lymphogranuloma venereum	0	0	*
Malaria	7	83	4
Measles	842	702	1082
Meningitis, meningococcal	9	12	12
Meningitis, Pfeiffer-bacillus	8	2	2
Meningitis, pneumococcal	7	3	6†
Meningitis, staphylococcal	0	1	0†
Meningitis, streptococcal	0	0	0†
Meningitis, other forms	0	1	2†
Meningitis, undetermined	2	3	2†
Mumps	319	669	670
Pneumonia, lobar	114	165	327
Poliomyelitis	18	11	7
Salmonella infections	10	5	5
Scarlet fever	663	523	978
Syphilis	238	459	433
Tuberculosis, pulmonary	223	164	239
Tuberculosis, other forms	16	10	18
Typhoid fever	3	2	5
Undulant fever	2	10	3
Whooping cough	730	598	598

*Made reportable December, 1943.
†Four-year average.

Comment

Diphtheria was at the highest prevalence for the month since 1933, the number of cases being more than four times the number recorded in December, 1945. Nearly 60 per cent of the cases were reported from Boston.

Pulmonary tuberculosis was at the highest level since 1942 but still below the median for the past seven years.

The late seasonal peak kept poliomyelitis above both the prevalence for December, 1945, and the median for the seven-year period.

Chicken pox, scarlet fever and whooping cough are just beginning to show trends toward higher levels. Only whooping cough, however, has risen above the median.

There has been a decline in the reporting of gonorrhea and syphilis, the former reaching the lowest level since 1942 and the latter the lowest since 1929.

Bacillary dysentery, measles and mumps were at low levels for the month.

Geographical Distribution of Certain Diseases

Anthrax was reported from: Peabody, 1; total, 1.

Diphtheria was reported from: Boston, 51; Bridgewater, 1; Brockton, 5; Greenfield, 2; Leominster, 2; Lowell, 3; Medford, 1; Methuen, 1; New Bedford, 4; Palmer, 7; Salem, 1; Somerville, 5; Tewksbury, 2; Wakefield, 1; Wilbraham, 1; Worcester, 1; total, 88.

Dysentery, bacillary, was reported from: Newton, 1; Northampton, 1; Springfield, 1; Wrentham, 1; total, 4.

Lymphocytic choriomeningitis was reported from: Cambridge, 1; Medford, 1; total, 2.

Malaria was reported from: Braintree, 1; Fall River, 1; Great Barrington, 1; Greenfield, 1; Murphy General Hospital, 1; Somerville, 1; Worcester, 1; total, 7.

Meningitis, meningococcal, was reported from: Boston, 3; Boxboro, 1; Easton, 1; Fall River, 2; Leominster, 1; Washington, 1; total, 9.

Meningitis, Pfeiffer-bacillus, was reported from: Boston, 2; Brockton, 1; New Bedford, 2; Rehoboth, 1; Worcester, 2; total, 8.

Meningitis, pneumococcal, was reported from: Boston, 1; Cambridge, 1; Cohasset, 1; Foxboro, 1; Northampton, 1; Worcester, 2; total, 7.

Meningitis, undetermined, was reported from: Medford, 1; North Adams, 1; total, 2.

Poliomyelitis was reported from: Ashburnham, 1; Athol, 1; Boston, 1; Blackstone, 1; Brookline, 2; Fall River, 2; Fitchburg, 1; Framingham, 1; Groveland, 1; Montague, 1; New Bedford, 3; Newton, 1; Taunton, 1; Wellesley, 1; total, 18.

Salmonella infections were reported from: Boston, 2; Chelsea, 2; Haverhill, 2; Lowell, 2; Melrose, 2; total, 10.

Septic sore throat was reported from: Amesbury, 14; Arlington, 1; Boston, 14; Lawrence, 1; Mansfield, 1; Merrimac, 5; Salem, 1; Williamstown, 1; total, 38.

Trichinosis was reported from: Cambridge, 1; Falmouth, 1; Framingham, 1; total, 3.

Tularemia was reported from: Boston, 1; Tisbury, 1; total, 2.

Typhoid fever was reported from: Leominster, 1; Marblehead, 1; Salem, 1; total, 3.

Undulant fever was reported from: Uxbridge, 1; Wellesley, 1; total, 2.

CORRESPONDENCE

PENICILLIN TREATMENT OF SYPHILIS

To the Editor: Relative to the excellent and timely editorial, "Syphilis and Penicillin," which appeared in the December 26 issue of the *Journal*, I should like to call attention to certain parts of it that are at variance with the instructions for the use of penicillin in the state co-operating venereal disease clinics, which are as follows.

All patients with early infectious syphilis (primary, secondary, and infectious relapses) and pregnant women with syphilis should be treated with 40,000 units of penicillin given intramuscularly every three hours, night and day, for seven and a half days or until a total of 2,400,000 units has been received, with 0.2 gm. bismuth subsalicylate (1.5 cc. Stabisol) on the first, third, fifth, seventh and ninth days. A Herxheimer reaction, with malaise and fever a few hours after onset of treatment, is to be expected in the majority of cases, but a generalized reaction of this nature is no reason to discontinue treatment.

Serologic and clinical follow-up should be done at the termination of treatment, every month for the first six months and quarterly thereafter until the end of the first year. If the serologic and clinical follow-up is negative, the patient should be discharged and advised to return once a year for check-up for the next five years.

In penicillin-treated cases of syphilis in which the periodic serologic and clinical follow-up indicates a relapse, the patient should be treated with 4,800,000 units of penicillin, given in 80,000-unit doses intramuscularly every three hours, night and day, for seven and a half days, with 0.2 gm. bismuth subsalicylate (1.5 cc. Stabisol) on the first, third, fifth, seventh and ninth days, unless contraindicated.

In cases in which periodic serologic and clinical examination gives evidence of resistance after the termination of the second course of penicillin, the patient should be referred to the Division of Venereal Diseases, Department of Public Health, for consultation as to further treatment.

All patients with late syphilis are being treated on a consultative basis, the consultation forms being reviewed by Dr. Solomon and his group at the Boston Psychopathic Hospital. This service is available to the private practitioner as well as to the co-operating clinics, and a request to this department should be made for further information on the same. This method of handling the treatment of patients with late syphilis is extremely valuable not only to the patient but also to the physician. Incidentally, there is available to co-operating clinics as well as to private practitioners consultatory information for infants and children who are infected with or suspected of having syphilis. Further information may be had by applying to this department.

This information is presented so that private practitioners and possibly the chiefs of the co-operating clinics who receive the *Journal* will not be confused.

Vlado A. Getting
Commissioner

Massachusetts Department of Public Health
State House
Boston

BOOK REVIEWS

Pediatric X-Ray Diagnosis: A textbook for students and practitioners of pediatrics, surgery and radiology. By John Caffey, M.D. 4°, cloth, 838 pp., with 710 illustrations. Chicago: The Year Book Publishers, Incorporated, 1945. $12.50.

The publication of Caffey's volume fulfills a need of long standing for a text and reference for both pediatrician and radiologist. The volume, based on twenty years' experience at the Babies' Hospital, is divided into the following six sections: "The Head and Neck," "The Thorax," "The Abdomen and Gastro-Intestinal Tract," "The Pelvis and Genito-Urinary Tract," "The Extremities" and "The Vertebral Column." Each section opens with a description of the normal roentgenologic appearance, and this is one of the valuable features of the book. The description of the various pathologic processes is thorough, although there are some rather important omissions, and the text is lucid and eminently readable. The reproductions and drawings, which are used freely, are excellent. The general format is satisfactory, and the bibliography adequate.

This book is recommended without hesitation for the library of every radiologist and pediatrician.

Large Scale Rorschach Techniques: A manual for the group Rorschach and multiple choice test. By M. R. Harrower-Erickson, Ph.D., and M. E. Steiner, M.A. 8°, cloth, 418 pp., with 157 tables. Springfield, Illinois: Charles C Thomas, 1945. $8.50.

The Rorschach (ink-blot) test for mental rating in its group application, originally designed for the military purposes of selection, classification and rehabilitation of personnel, is discussed in detail in this volume. The first part comprises a brief history of the development of the group procedure, its uses and its technical administration. The second is devoted to an experimental investigation on 340 subjects, providing 8526 responses. The results are presented in both graphic and tabular form. The third describes the multiple-choice test derived from the large mass of experimental material. This short, objective test is designed for the use of psychologists, psychiatrists, educators, social workers and probation officers without any Rorschach training. In this part will be found special chapters on military psychiatric differentiation. The fourth part is composed of lists of the content of responses, intended for reference purposes.

Plaster of Paris Technique in the Treatment of Fractures and Other Injuries. By T. B. Quigley, M.D. 8°, cloth, 107 pp., with 103 illustrations. New York: The Macmillan Company, 1945. $3.50.

This booklet describes, in a concise manner, the application of plaster of Paris to all parts of the body. Simple methods are given that require no special apparatus. The discussion of padding and of the complications that may arise when plaster casts are used is especially well done. Only one method is presented, which is probably an advantage to the novice, since it often requires long experience to select the most efficient technic for different disabilities. Whereas plaster can be used as described for splinting small joints like those of the finger, tin or aluminum is usually found to be much less awkward to manage.

Plaster technic is described for fractures and other injuries to the limbs only, but the technic can be applied to many other disabilities. This is an excellent book and should prove helpful to those who use this type of treatment.

Our Inner Conflicts: A constructive theory of neurosis. By Karen Horney, M.D. 8°, cloth, 250 pp. New York: W. W. Norton and Company, Incorporated, 1945. $3.00.

This book, by an author who has proved her value as an interpreter of psychiatry, particularly the psychoneuroses, by her ability to present the material clearly and concisely for general reading, follows the tendency that has been characteristic of her writings in the past. The author has a clear concept of the subject and presents it in a comprehensive manner. She points out the harm that neurotic conflicts can inflict on the personality: to resolve them, more than rational decision, evasion or the exertion of will power is necessary. They can be cured only by changing those conditions within the personality that draw the conflict into being. Dr. Horney's method of doing this is fully expounded. She is willing, however, to take an even broader view of psychotherapy and writes as follows:

> Fortunately analysis is not the only way to resolve inner conflicts. Life itself still remains a very effective therapist. Experience of any one of a number of kinds may be sufficiently telling to bring about personality changes. It may be the inspiring example of a truly great person; it may be a common tragedy which, by bringing the neurotic in close touch with others, takes him out of his egocentric isolation; it may be association with persons so congenial that manipulating or avoiding them appears less necessary. In other instances the consequences of neurotic behavior may be so drastic or of such frequent occurrence that they impress themselves on the neurotic's mind and make him less fearful and less rigid.

This, indeed, is sound psychotherapy and a point often overlooked by many writers on the subject. This book in general is highly recommended.

Pathology of Tropical Diseases: An atlas. By J. E. Ash, M.D. and Sophie Spitz, M.D. 4°, cloth, 350 pp., with 941 illustrations. Philadelphia: W. B. Saunders Company, 1945. $8.00

This volume presents an array of excellent photographic illustrations of many of the diseases of the tropics. The text that accompanies the illustrations is of uneven quality. That part dealing with pathology is excellent, but other parts are replete with statements that are of doubtful validity, misleading or incorrect, and these detract from the value of the book.

The Eternal Ones of the Dream: A psychoanalytic interpretation of Australian myth and ritual. By Géza Róheim, Ph.D. 8°, cloth, 270 pp. New York: International Universities Press, 1945. $4.50.

An anthropologic study from a psychoanalytical orientation of various Australian myths, this book is divided into an introduction and twelve chapter headings, with a final summary and conclusion. There also appears a page of illustrations of several ritualistic ceremonies, as well as addenda depicting several myths and ceremonial objects. Etymology, presentation and interpretation of native word symbols are frequent. This lends a heavy air of technicality to the work but makes for difficult reading to the uninitiate in philology. The reasonableness of the author's interpretations depends on the reader's psychoanalytic leanings rather than on objective data. An example is the following statement: "... the eternal ones of the dream it is we who deny decay and aggression and object-loss, and who guard eternal youth and reunion with the mother."

General and Plastic Surgery, with Emphasis on War Injuries. By J. Eastman Sheehan, M.D. 8°, cloth, 345 pp., with 4[illegible] illustrations. New York and London: Paul B. Hoeber, Incorporated, 1945. $6.75.

This book, which was published in 1945, was not reviewed until October, 1946, and certain material is outdated by more recent developments and concepts. One example is the recommendation that sulfonamide ointments be used in the treatment of burns, and another, that sulfonamide insufflation be used previous to closure of wounds.

This book, however, which has more to do with plastic surgery and the surgery of trauma than with general surgery, introduces and summarizes certain British contributions that should be of use in this country. Wounds are discussed generally and under the regions of the body in which they occur. An interesting section is devoted to war weapons and their methods of injuring and the injuries thus produced.

The volume is profusely illustrated with carefully selected diagrams and photographs.

Plastic surgeons and those interested in trauma may wish to find this book a useful summary of the treatment of war wounds during World War II, particularly the reconstructive aspects. It cannot be called a summary of all the useful methods developed during the war, however, for the procedures described are largely based on experiences in the Spanish Civil War and with the British in World War II.

Amputation Prosthesis: Anatomic and physiologic considerations, with principles of alignment and fitting designed for the surgeon and limb manufacturer. By Atha Thomas, M.D., and Chester C. Haddan. 8°, cloth, 305 pp., with 207 illustrations. Philadelphia: J. B. Lippincott Company, 1945. $8.00.

World War II, like all wars, produced a revival of interest in amputations and prostheses. More than 15,000 members of the armed forces of the United States lost an arm or a leg. But it is not generally appreciated that forty thousand major amputations, requiring prostheses, are carried out in this country every year. In the services the liaison among surgeon, physical therapist and limb fitter is close and efficient; in civil practice it is not infrequently casual and ineffective. This book, written jointly by a well known surgeon and by the president of the Association of Limb Manufacturers of America, should go far toward bridging this gap. It fills a long felt need in presenting in one profusely illustrated and well written volume the essentials of modern management of amputations. The extensive British experience at Roehampton between the two wars is freely drawn on, and an excellent bibliography is appended to each chapter.

In the Doctor's Office: The art of the medical assistant. By Esther J. Parsons. Illustrations by Jean McConnell. 12°, cloth, 300 pp., with illustrations. Philadelphia: J. B. Lippincott Company, 1945. $2.00.

This manual, which was written primarily for the physician's assistant, the receptionist, secretary, nurse and laboratory technician, discusses in detail her relations with the physician and his patients. The important subjects of handling patients in the office and the conduct of telephonic service are considered frankly, as well as the personality, character and health of the assistants. The care of office equipment, the keeping of records, office bookkeeping and correspondence are discussed. An important chapter on emergency care in the absence of the physician is included. The material is well organized, and the text well written in an easy style. The type is large and printed on a good soft paper, easy to read and to handle. This manual should prove profitable to both physicians and assistants.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Science and Seizures: New light on epilepsy and migraine. By William G. Lennox, M.D., Sc.D. (hon.), assistant professor of neurology, Harvard Medical School, and visiting neurologist, Boston City Hospital. Second edition. 12°, cloth, 258 pp., with 10 illustrations. New York: Harper and Brothers, 1946. $2.00.

The first edition of this popular book on epilepsy was published in 1941, and since that time it has been found necessary to make seven reprintings. In this second edition, the section dealing with medication has been rewritten, including a discussion of the use of Tridione. The book should prove of value to all persons coming into contact with sufferers of epilepsy and migraine.

How A Baby Grows: A story in pictures. By Arnold Gesell, M.D., director, Clinic of Child Development, Yale University. 4°, cloth, 80 pp., with over 800 photographs arranged and interpreted with the assistance of Katherine G. Walden, A.B. New York and London: Harper and Brothers, 1945. $2.00.

This new type of book consists of an atlas, with a simple, explanatory text, tracing the changes in a child's development during the first five years of life. The pictures are arranged to show instantly and vividly how the infant grows from day to day and month to month and why he acts as he does. Part one shows how the baby gains control of his body, and part two portrays the growth of his mental abilities and personality. The pictures, which are based on the average trends of development, do not portray individual variations.

Trauma of the Central Nervous System: Proceedings of the Association for Research in Nervous and Mental Disease, December 17 and 18, 1943, New York. 8°, cloth, 679 pp., with 243 illustrations and 44 tables. Research Publications, Volume XXIV. Baltimore: The Williams and Wilkins Company, 1945. $8.00.

This volume contains twenty-seven papers concerning trauma of the head and brain. The first paper, by Dr. Fred A. Metler, is a history of cranial trauma from the earliest times to the nineteenth century. The other papers are devoted to the physiology, histology, pathology, diagnosis and aftereffects of head injuries. This volume should be in all medical libraries and should prove of value to surgeons interested in brain surgery.

New Drugs. By Arthur D. Herrick. With a foreword by Austin E. Smith, M.D., secretary, Council on Pharmacy and Chemistry, American Medical Association. 8°, cloth, 303 pp. New York: Revere Publishing Company, 1946. $4.00.

The title of this new book is misleading, since it does not list and consider new drugs but concerns the regulation of new drugs under federal and municipal control. The first part of the book consists of a thorough analysis of the federal Food and Cosmetic Act of 1938 as it relates to drugs and discusses thoroughly the testing of new drugs for the purpose of determining their safety. The various legal procedures relating to the act are briefly outlined.

An appendix of four parts includes a report of the Secretary of Agriculture on deaths due to elixir sulfanilamide. This report was made in response to Senate Resolution 1944 of November 16, 1937, and was published as Senate Document No. 124, 75th Congress, 2nd Session. During September and October, 1937, at least seventy-three persons died as a direct result of taking the elixir. Twenty other persons died, but the exclusive responsibility of the drug was not established. The ninety-three deaths occurred in fifteen states reaching from Virginia to California. Two hundred and forty gallons were manufactured in Tennessee, and owing to the diligence and quick action of the Food Drug Administration the entire amount of unused elixir was retrieved, and this serious

The Journal lacks extra copies of the February 21, October 3 and November 14, 1946, issues. If any subscribers who do not bind their copies have the above-mentioned issues on hand, the Journal will gladly pay 15 cents for each copy left at or mailed to its office (8 Fenway, Boston 15).

epidemic of drug poisoning was brought to an end. Appendix B consists of selected articles bearing on drugs taken from the Federal Drug and Cosmetic Acts and Regulations. Appendix C is a summary of drug legislation now in force in eleven states and in New York City. The work concludes with the official rules of the Council on Pharmacy and Chemistry of the American Medical Association.

This new work should be in the collection of all public, medical and legal libraries and should be valuable for all persons interested in pharmacy and drug manufacturing.

Industrial Toxicology. By Alice Hamilton, M.D., and Rutherford T. Johnstone, M.D., director, Department of Occupational Diseases, Golden State Hospital, California. (Reprinted from *Oxford Loose-Leaf Medicine*, with the same page numbers as in that work.) 8°, cloth, 65 pp. New York: Oxford University Press, 1946. $2.50.

This short monograph by recognized authorities summarizes the pathology, diagnosis, treatment and prevention of industrial poisoning. A long bibliography is appended to the text. The publishers in reprinting this important contribution have made it possible for interested persons to have the monograph without subscribing to *Oxford Loose-Leaf Medicine*. The monograph is recommended for all medical and public libraries and to all persons interested in industrial poisoning.

NOTICES

ANNOUNCEMENT

Dr. Irving L. Pavlo, having returned from military service, announces the opening of his office at 469 Beacon Street, Boston, for the practice of ophthalmology.

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, February 18, at twelve noon. Dr. Reginald H. Smithwick will speak on "The Surgical Treatment of Hypertension."

Physicians are cordially invited to attend.

BOSTON GASTROENTEROLOGICAL SOCIETY

The Boston Gastroenterological Society will hold a luncheon meeting for members and their guests in the Harvard Club on Wednesday, February 19, at twelve noon. Dr. Dwight O'Hara will speak on "The Activities of the Massachusetts Medical Society."

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The regular meeting of the New England Society of Physical Medicine will be held at the Hotel Kenmore, Boston, on Wednesday, February 19, at 8 p.m.

PROGRAM

Exercises for Bed Patients, Medical and Surgical. Dr. J. Wayne MacFarland, of Washington, D. C., editor of *Life and Health* and vice-chairman on physical medicine, Southern Medical Association.

Physicians, students, physical therapists and nurses are cordially invited to attend this meeting.

NEW ENGLAND PATHOLOGICAL SOCIETY

The next meeting of the New England Pathological Society will be held on Thursday, February 20, at the Beth Israel Hospital, Boston. The afternoon slide seminar will be held at 4 p.m. Dinner will be served at the hospital, and the evening meeting will be held in the auditorium at 8 p.m. Dr. Frank W. Foote will speak on the subject "Benign Proliferative Lesions of the Breast."

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

The three hundred and seventy-fifth meeting of the New England Ophthalmological Society will be held on Wednesday, February 19, at the Massachusetts Eye and Ear Infirmary, Boston.

PROGRAM

9:00 a.m.–12:00 m. Operating Clinic. Staff members.

2:30–3:30 p.m. Presentation of cases.

4:00–5:30 p.m. Instructional Course. "Pathology of the Conjunctiva."

8:00 p.m. Business Meeting.

8:15 p.m. "Twenty-nine Cases of Rheumatoid Iritis." Dr. Lloyd Mills.

8:45 p.m. "The Surgical Treatment of Strabismus in Children." Dr. Maynard C. Wheeler, of the Eye Institute, Columbia Medical Center, New York City.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, FEBRUARY 20

FRIDAY, FEBRUARY 21

*9:00–10:00 a.m. The Mechanisms of Hemoglobinuria in Thermal Burns. Dr. Thomas Hale Ham. Joseph H. Pratt Diagnostic Hospital.

*10:00 a.m.–12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.

MONDAY, FEBRUARY 24

*12:15–1:15 p.m. Clinicopathological Conference. Peter Bent Brigham Hospital.

TUESDAY, FEBRUARY 25

*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

WEDNESDAY, FEBRUARY 26

*9:00–10:00 a.m. The Use of Streptomycin in Tuberculosis. Dr. Lowrey F. Davenport. Joseph H. Pratt Diagnostic Hospital.

*11:00 a.m.–12:00 m. Medical Clinic. Amphitheater, Children's Hospital.

*12:00 m. Clinicopathological Conference. (Children's Hospital.) Amphitheater, Peter Bent Brigham Hospital.

*2:00–3:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

*7:15 p.m. Graduate Seminar in Pediatrics. Children's Medical Service, Amphitheater 3A, Massachusetts General Hospital.

*Open to the medical profession.

OCTOBER 11–MAY 14. Metropolitan State Hospital. Page 398, issue of September 12.

FEBRUARY 18. South End Medical Club. Notice above.

FEBRUARY 19. New England Society of Physical Medicine. Notice above.

FEBRUARY 19. Boston Gastroenterological Society. Notice above.

FEBRUARY 19. New England Ophthalmological Society. Notice above.

FEBRUARY 20. New England Pathological Society. Notice above.

FEBRUARY 26. Tufts Alpha Omega Alpha. Page 156, issue of January 2.

MARCH 11. Harvard Medical Society. Amphitheater, Peter Bent Brigham Hospital. 8:00 p.m.

MARCH 13. Cornell Medical Alumni Day. Page 156, issue of January 2.

MARCH 13. What We Have Learned from the Study Through the United States of Child Health Service. Dr. Warren R. Sisson. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

APRIL 28–MAY 2. American College of Physicians. Page 206, issue of August 8.

MAY 20–22. Massachusetts Medical Society. Annual meeting. Hotel Statler, Boston.

JUNE 9–13. American Medical Association. Page 698, issue of November 7.

JUNE 30–JULY 3. American Urological Association. Hotel Statler, Buffalo.

SEPTEMBER 8–12. Third American Congress on Obstetrics and Gynecology. Page 636, issue of October 24.

DISTRICT MEDICAL SOCIETY

PLYMOUTH

FEBRUARY 20. Moore Hospital, Brockton.

MARCH 20. Goddard Hospital, Brockton.

APRIL 17. State Farm, Bridgewater.

MAY 15. Lakeville Sanatorium, Lakeville.